EXHIBIT 40


NIPC
National Initiative on Pain Control®
CHRONIC OPIOID THERAPY
Understanding Risk While Maximizing Analgesia
CHRONIC PAIN
OAT
SOAPP
OPIOID BENEFITS
OPIOID RISKS
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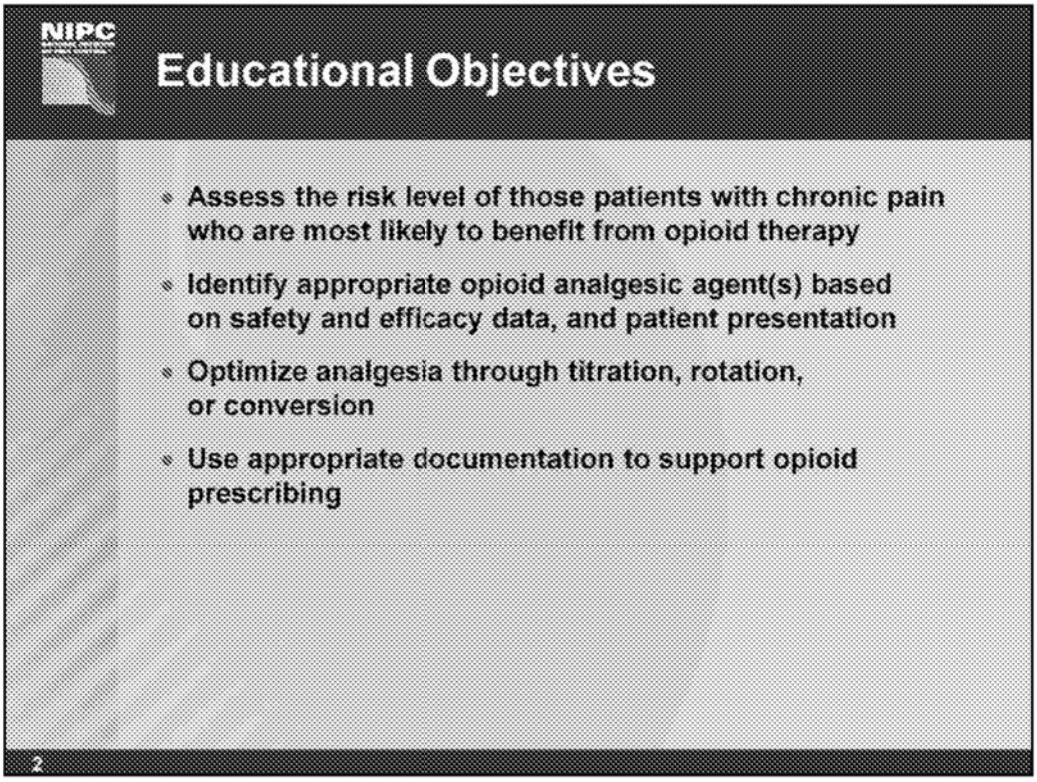
Salt Lake City, Utah
Professional Postgraduate Services®


NIPC
Educational Objectives
Assess the risk level of those patients with chronic pain who are most likely to benefit from opioid therapy
Identify appropriate opioid analgesic agent(s) based on safety and efficacy data, and patient presentation
Optimize analgesia through titration, rotation, or conversion
Use appropriate documentation to support opioid prescribing
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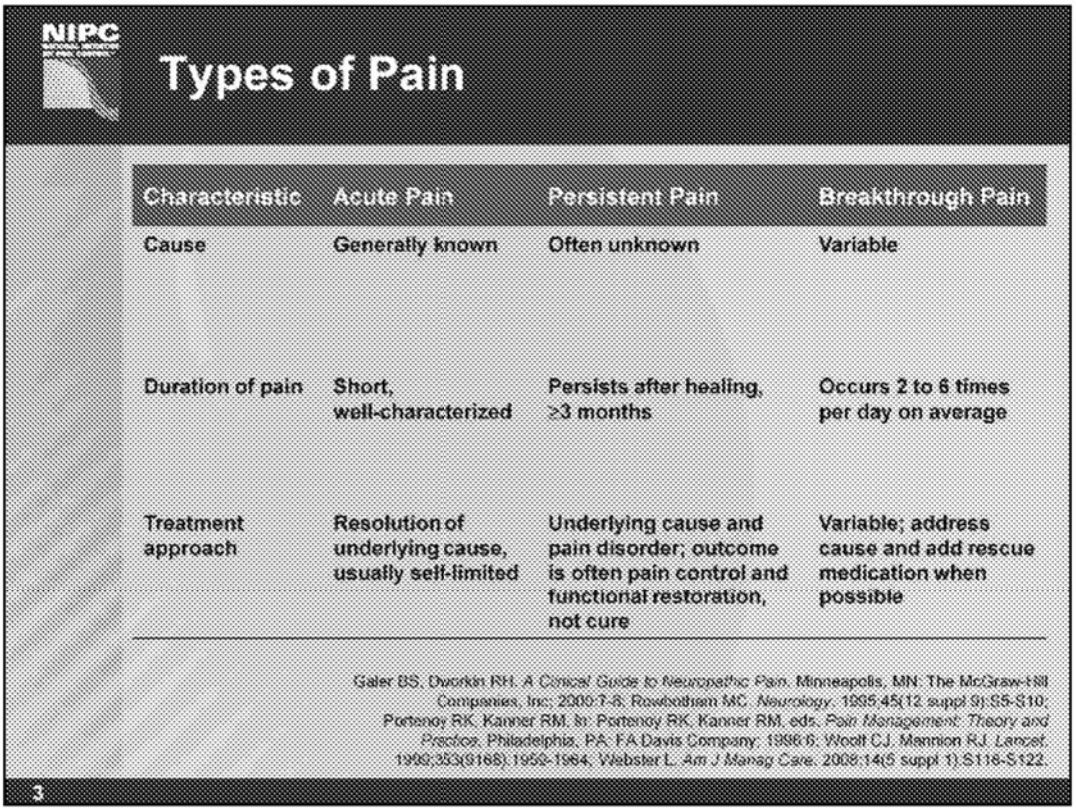


The causes of acute pain are often known, but the causes of persistent pain and its associated symptoms are not well understood.[1]

The pain experienced by patients with acute pain often can be alleviated. In general, the duration of acute pain is brief and has been well characterized.[1] The time course of persistent pain, however, is usually indeterminate, and patients with persistent pain are often refractory to treatment.[2]

One definition of persistent pain is pain that has persisted beyond the time of normal healing; for research purposes, however, persistent pain is often defined as pain that has endured at least 3 (sometimes 6) months.[3]

Because persistent pain can almost never be cured,[4] optimal treatment usually involves helping the patient restore function and supporting a patient's coping by utilizing approaches that minimize pain, maximize quality of life (QOL), improve sleep, and enable patients to return to work and perform their regular activities.[3,4]

Breakthrough pain[5]

- Occurs against a background of otherwise controlled chronic cancer or noncancer pain
- Occurs several times daily
- Episodes peak within 3 to 30 minutes
- 3 types: idiopathic, incident (has identifiable cause), end-of-dose failure
- Underlying cause should be addressed to the extent possible; rescue medication should be given in addition baseline pain control medication

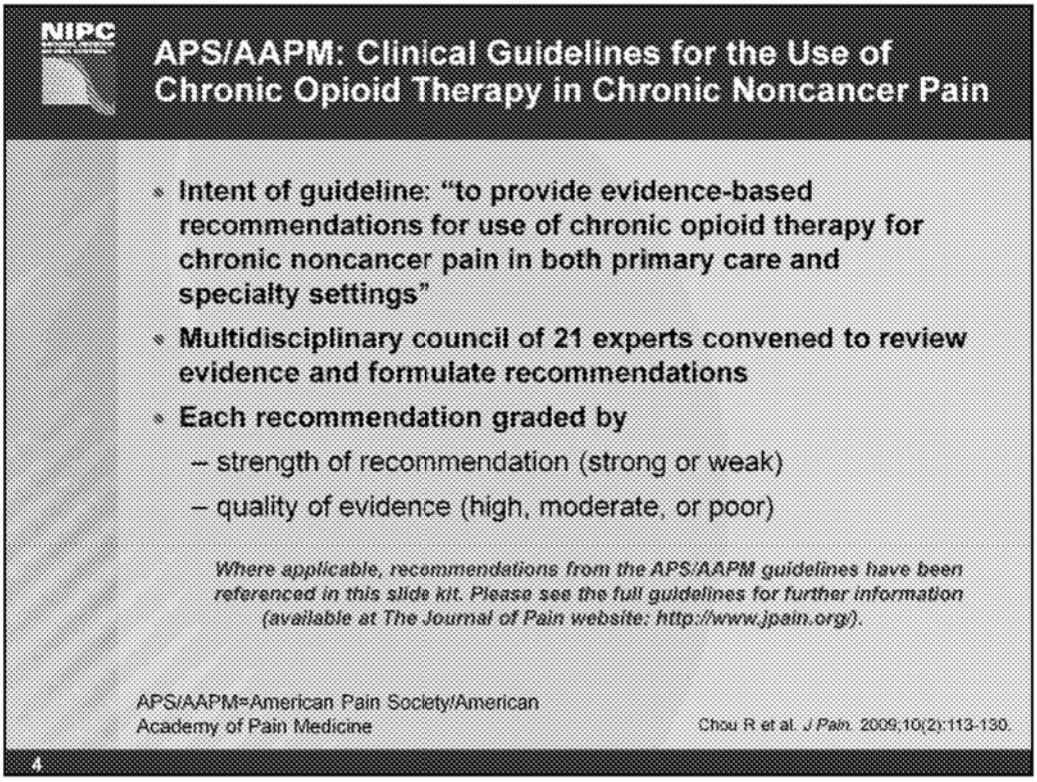
Galer BS, Dworkin RH. *A Clinical Guide to Neuropathic Pain*. Minneapolis, Minn: The McGraw-Hill Companies, Inc; 2000:7-8.

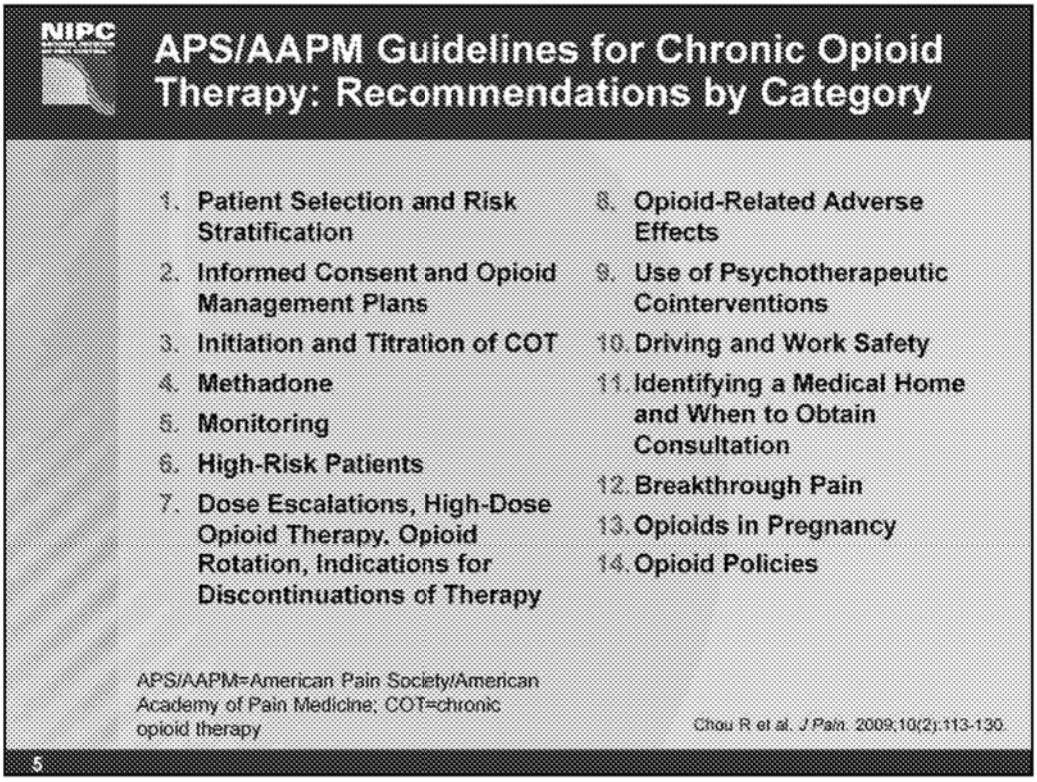
Rowbotham MC. Chronic pain: from theory to practical management. *Neurology*. 1995;45(12 suppl 9):S5-S10.

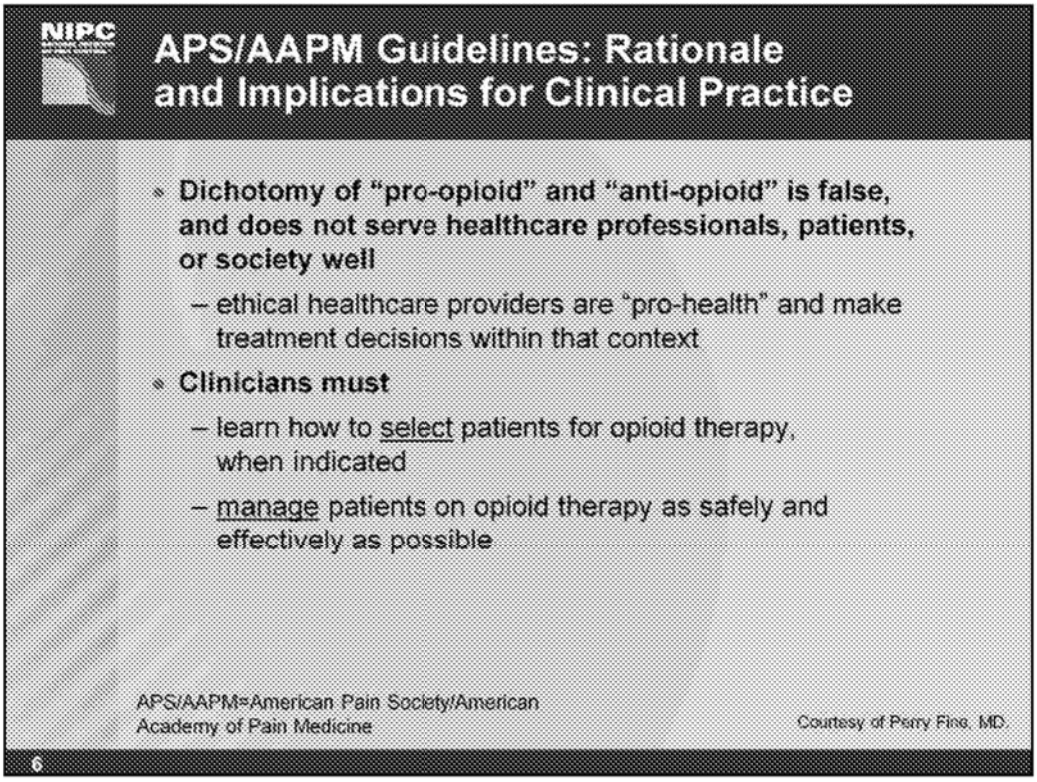
Portenoy RK, Kanner RM. Definition and assessment of pain. In: Portenoy RK, Kanner RM, eds. *Pain Management: Theory and Practice*. Philadelphia, Pa: FA Davis Company. 1996:6.

Woolf CJ, Mannion RJ. Neuropathic pain: aetiology, symptoms, mechanisms, and management. *Lancet*. 1999;353(9168):1959-1964.

Webster L. *Am J Manag Care*. 2008;14(5 Suppl 1):S116-S122.






NIPC
APS/AAPM Guidelines: Rationale and Implications for Clinical Practice
Dichotomy of "pro-opioid" and "anti-opioid" is false, and does not serve healthcare professionals, patients, or society well
– ethical healthcare providers are "pro-health" and make treatment decisions within that context
Clinicians must
– learn how to select patients for opioid therapy, when indicated
– manage patients on opioid therapy as safely and effectively as possible
APS/AAPM=American Pain Society/American Academy of Pain Medicine
Courtesy of Perry Fine, MD.
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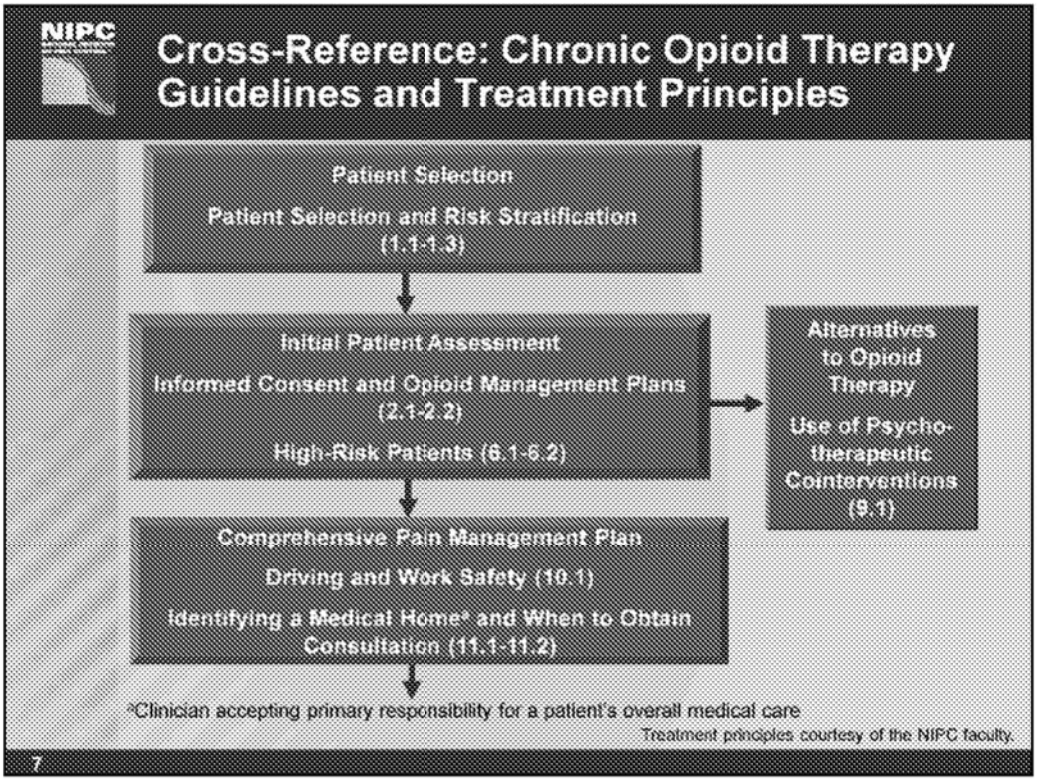
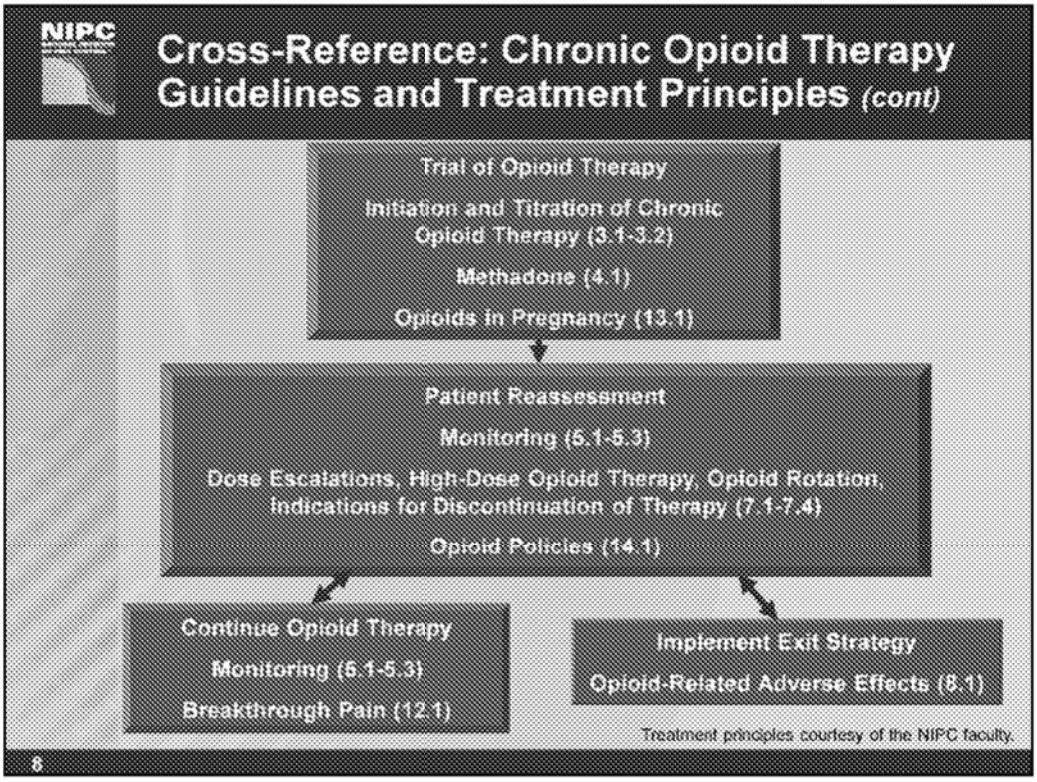


This algorithm has been created to assist in decision making about opioid therapy for chronic pain. The algorithm guides the participant through patient selection and assessment, what to consider in starting a trial of opioids, alternatives to opioid therapy, ongoing reassessment, developing an exit strategy, as well as conversion and rotation as part of the treatment strategy.



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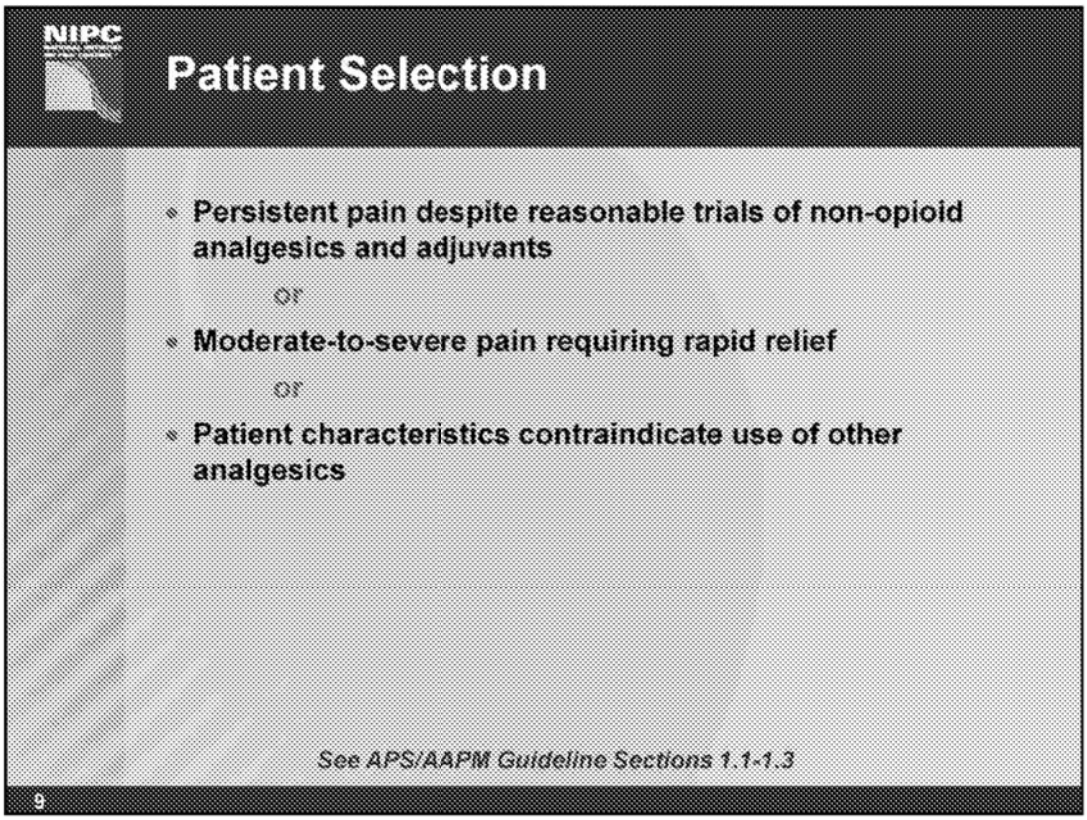


Opioids are an important class of therapeutic agents used to manage chronic pain.

Opioids are generally recommended to reduce the level of moderate to severe pain.

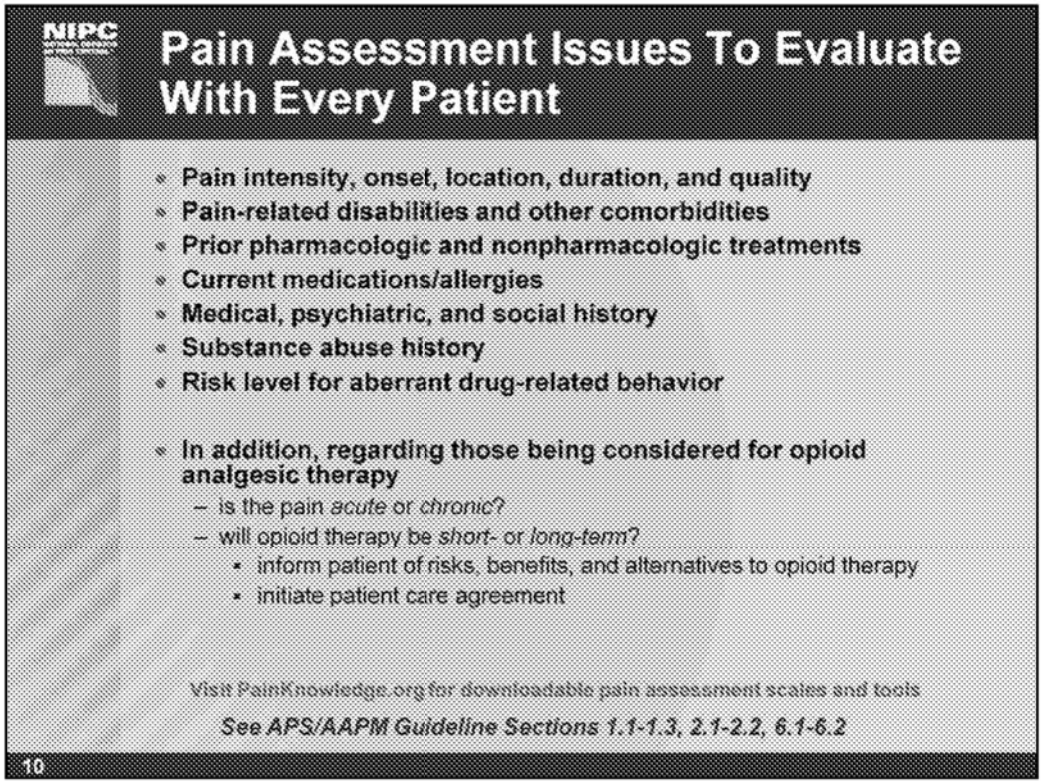
Opioids should be considered if reasonable, conservative therapy has been tried and has not been found to provide adequate relief.

Nonopioid analgesics include acetaminophen and nonsteroidal anti-inflammatory drugs (nonselective agents and selective COX-2 inhibitors).

Adjuvants include specific medications for neuropathic pain (antidepressants, anticonvulsants, miscellaneous agents), specific medications for cancer-related pain (bisphosphonates, radioisotopes, steroids), and medications for bowel spasms.

American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain. Consensus statement from the American Academy of Pain Medicine and the American Pain Society. *Clin J Pain*. 1997;13:6-8.

Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. *Adv Ther*. 2000;17:70-83.



Gaps in knowledge, negative attitudes toward prescribing opioids, inadequate assessment kills, and timidity in prescribing are barriers that clinicians may unwittingly bring to clinical encounters with patients. The problem might begin with the low priority given to pain treatment in medical schools and residency training programs.

Opioid therapy entails a number of risks for patients, but these potential problems can be prevented or circumvented.

Documentation is critical and should include the initial evaluation, substance abuse history, psychosocial issues, pain/pain relief, side effects, functional outcomes, and continuing monitoring. Regular discussions with family members about the patient's condition and use of opioids can improve the accuracy of monitoring.

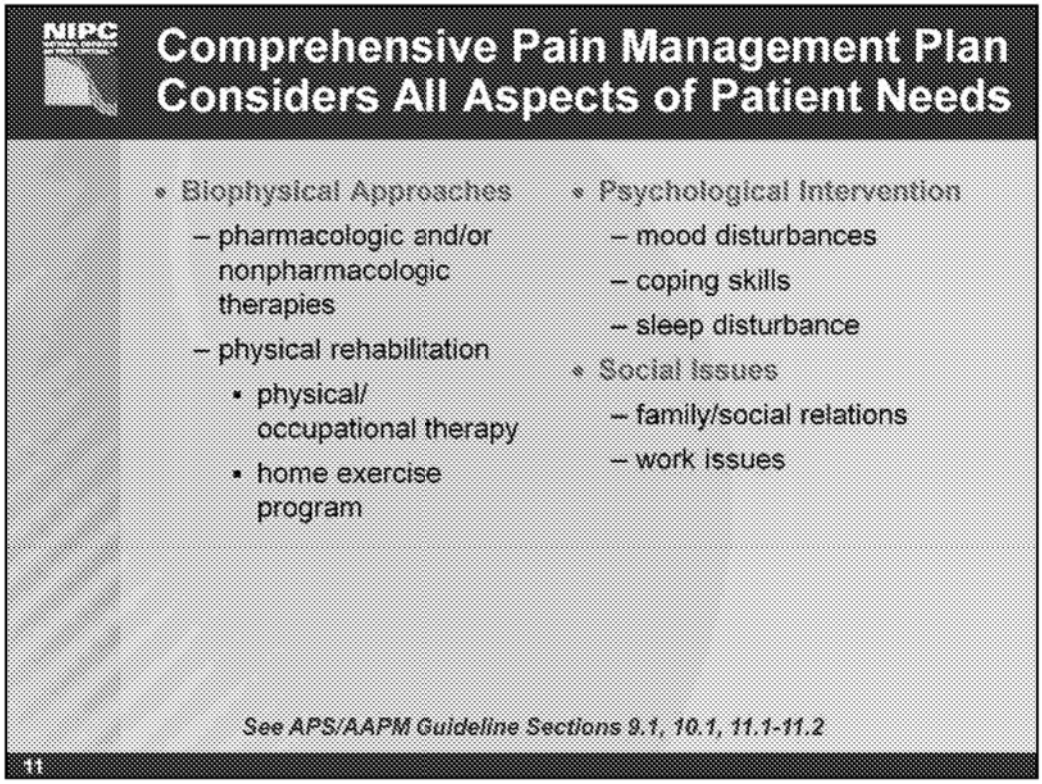
The Federation of State Medical Boards' model guidelines for the use of controlled substances for the treatment of pain require that a complete medical history and physical examination must be conducted and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function, and history of substance abuse.

Federation of State Medical Boards. Model guidelines for the use of controlled substances for the treatment of pain. Available at: http/www.csam-asam.org/pain_treatment_guidelines.htm. Accessed 9/02/03.

Glajchen M. Chronic pain: treatment barriers and strategies for clinical practice. *J Am Board Fam Pract.* 2001;14:211-218.

Joint Commission on Accreditation of Health Organizations. Pain assessment and management standards—hospitals. Available at: http://www.jcrine.com/subscribers/perspectives.asp?durki=3243&site=10&return=2897. Accessed 9/02/03.

Pappagallo M. Aggressive pharmacologic treatment of pain. *Rheum Dis Clin North Am.* 1999;25:193-213.



Based on thorough assessment of a patient with chronic pain, a clinician can develop a comprehensive management plan that may or may not emphasize pharmacologic therapy among other multimodal treatment approaches.

The best use of multimodal treatment

When screening programs indicate the presence of disorders such as depression or anxiety

When treating a chronically dysfunctional patient, angry patient, or one with personality disorders.

Psychological interventions are aimed at the devastating psychological effects chronic pain can have on patients.

Chronic pain can undermine their self-esteem and motivation and cause them to feel both helpless and hopeless.

Psychological interventions include:

active listening

family therapy

group therapy

supportive psychotherapy

cognitive behavioral therapy

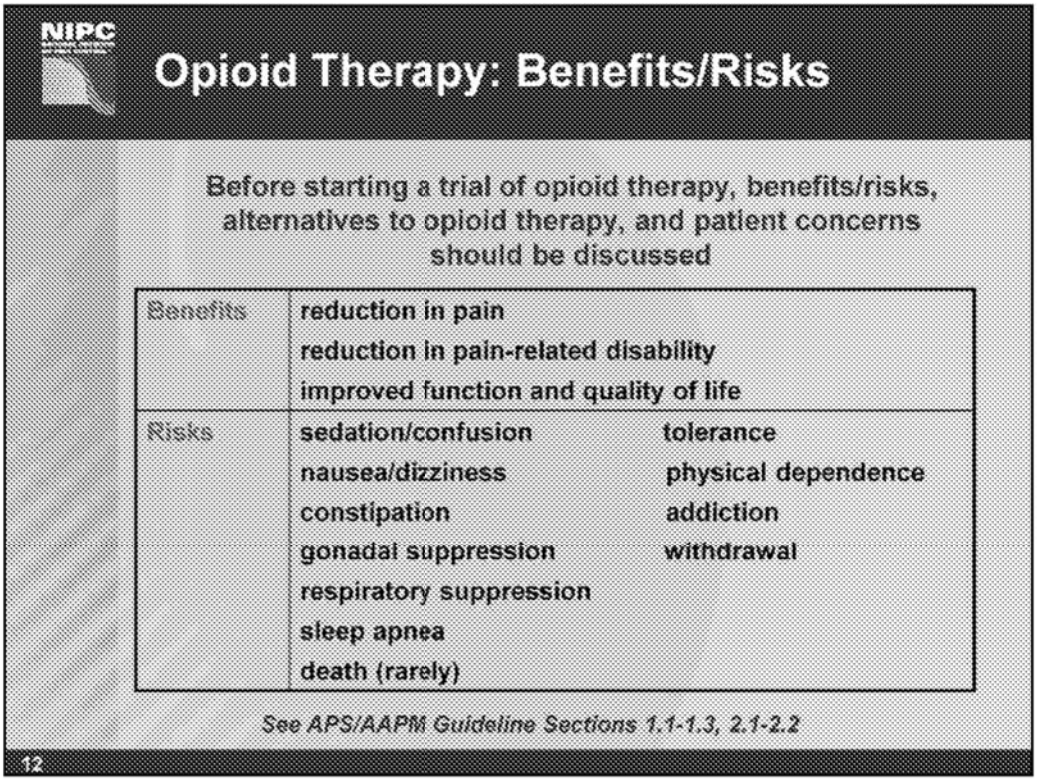
Most often these are provided in the context of other therapy, including pharmacologic and rehabilitative.

Psychological intervention is an integral part of the routine management of chronic pain as it improves patients' coping skills and their ability to relax and sleep without interruption.[1]

Support for patients with chronic pain can come from many sources, including patients' families. It is important for families to understand fully the stress and despair the patient feels.

Social and rehabilitative issues in chronic pain focus on its social and environmental determinants. Treatment typically works with each individual and family members to change the consequences of a pain lifestyle and focus on well behavior, increased functionality, and normal socialization and activities.

1. Russo CM. Pain: Control. *Encyclopedia of Life Sciences*. Macmillan Publishers Ltd; 2001.


NIPC
Opioid Therapy: Benefits/Risks
Before starting a trial of opioid therapy, benefits/risks, alternatives to opioid therapy, and patient concerns should be discussed
Benefits
reduction in pain
reduction in pain-related disability
improved function and quality of life
Risks
sedation/confusion
nausea/dizziness
constipation
gonadal suppression
respiratory suppression
sleep apnea
death (rarely)
tolerance
physical dependence
addiction
withdrawal
See APS/AAPM Guideline Sections 1.1-1.3, 2.1-2.2
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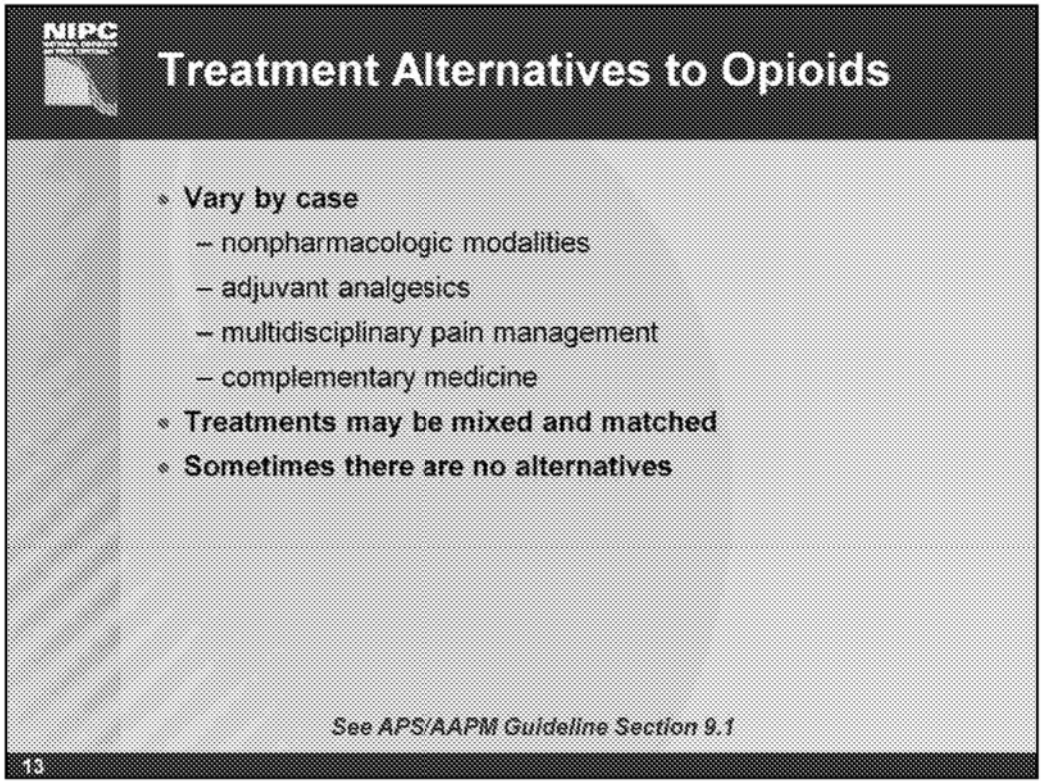


Alternatives to opioids for persistent pain
- Anticonvulsants
- Tricyclic antidepressants
- Topical medications

Adjuvant analgesics
- Acetaminophen
- Ketamine

Interventional treatments
- Neural blockade
- Stimulatory techniques (spinal cord stimulation; peripheral nerve stimulation)

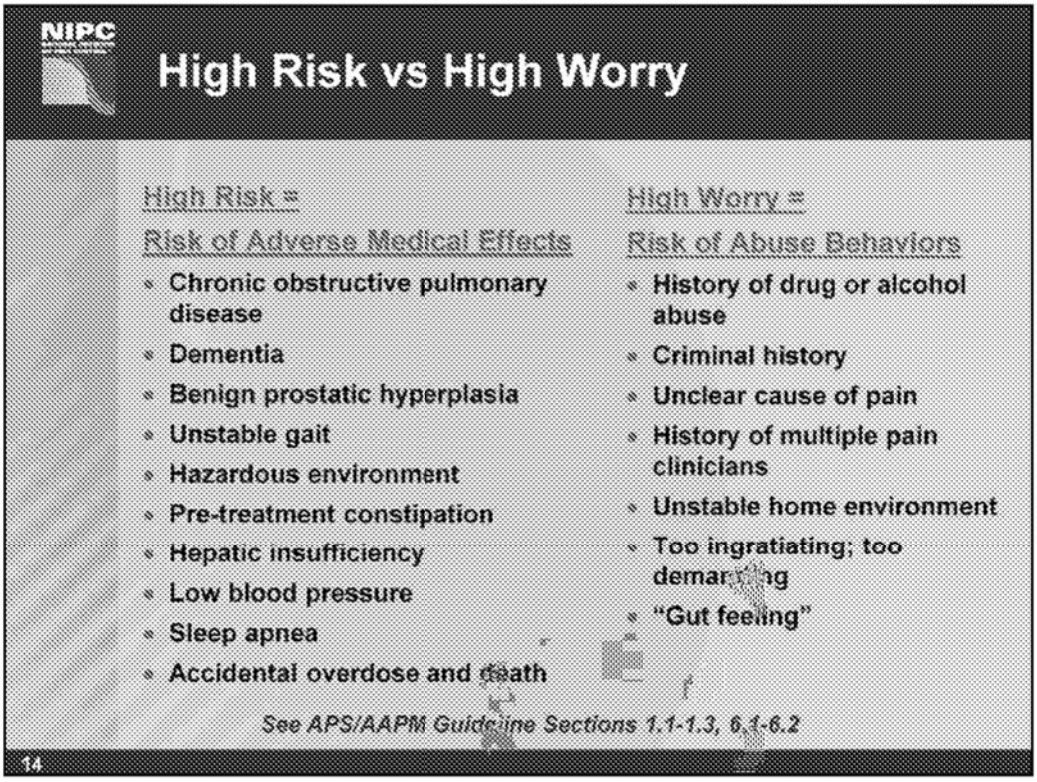
Nonpharmacological therapies
- Biofeedback
- Relaxation therapy
- Cognitive/behavioral strategies
- Acupuncture

Bell R, Eccleston C, Kalso E. Ketamine as an adjuvant to opioids for cancer pain. *Cochrane Database Syst Rev*. 2003;(1):CD003351.

Carter GT, Galer BS. Advances in the management of neuropathic pain. *Phys Med Rehabil Clin N Am*. 2000;12:447-459.

Ferrell B, Herr K, Epplin J, et al. The management of persistent pain in older persons. *J Am Ger Soc*. 2002;50:1-20.

Galer BS, Dworkin RH. *A Clinical Guide to Neuropathic Pain*. Minneapolis, MN: McGraw-Hill Companies Inc; 2000:120,135.


NIPC
High Risk vs High Worry
High Risk =
Risk of Adverse Medical Effects
Chronic obstructive pulmonary disease
Dementia
Benign prostatic hyperplasia
Unstable gait
Hazardous environment
Pre-treatment constipation
Hepatic insufficiency
Low blood pressure
Sleep apnea
Accidental overdose and death
High Worry =
Risk of Abuse Behaviors
History of drug or alcohol abuse
Criminal history
Unclear cause of pain
History of multiple pain clinicians
Unstable home environment
Too ingratiating; too demanding
"Gut feeling"
See APS/AAPM Guideline Sections 1.1-1.3, 6.1-6.2
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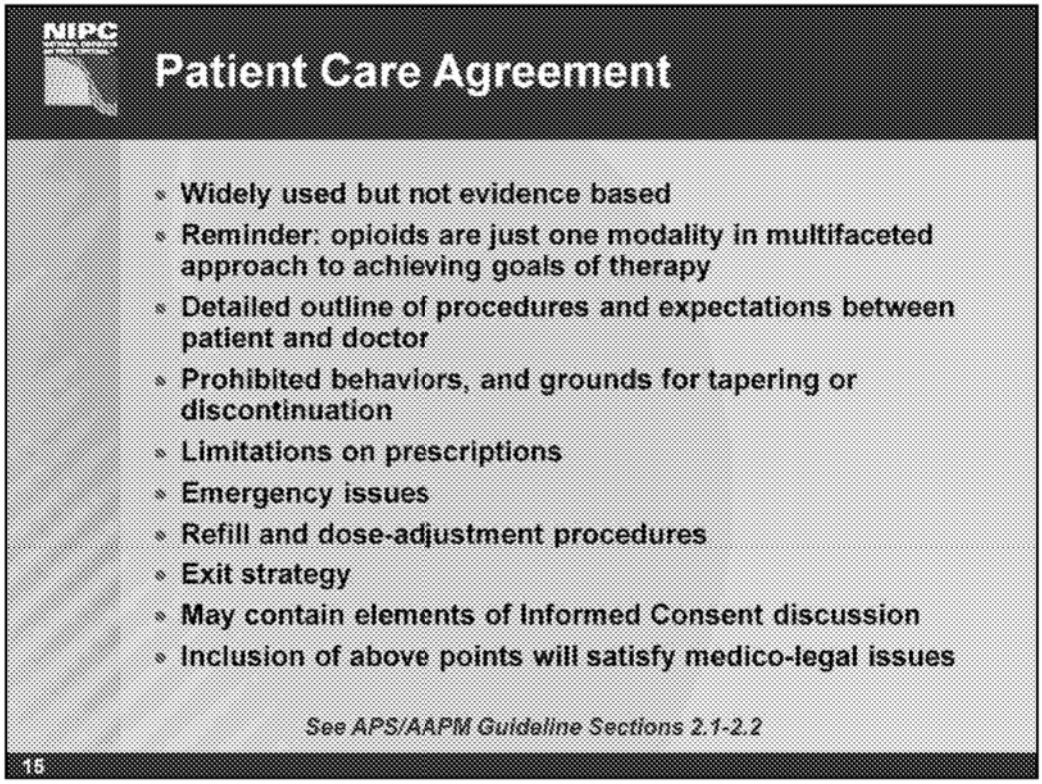


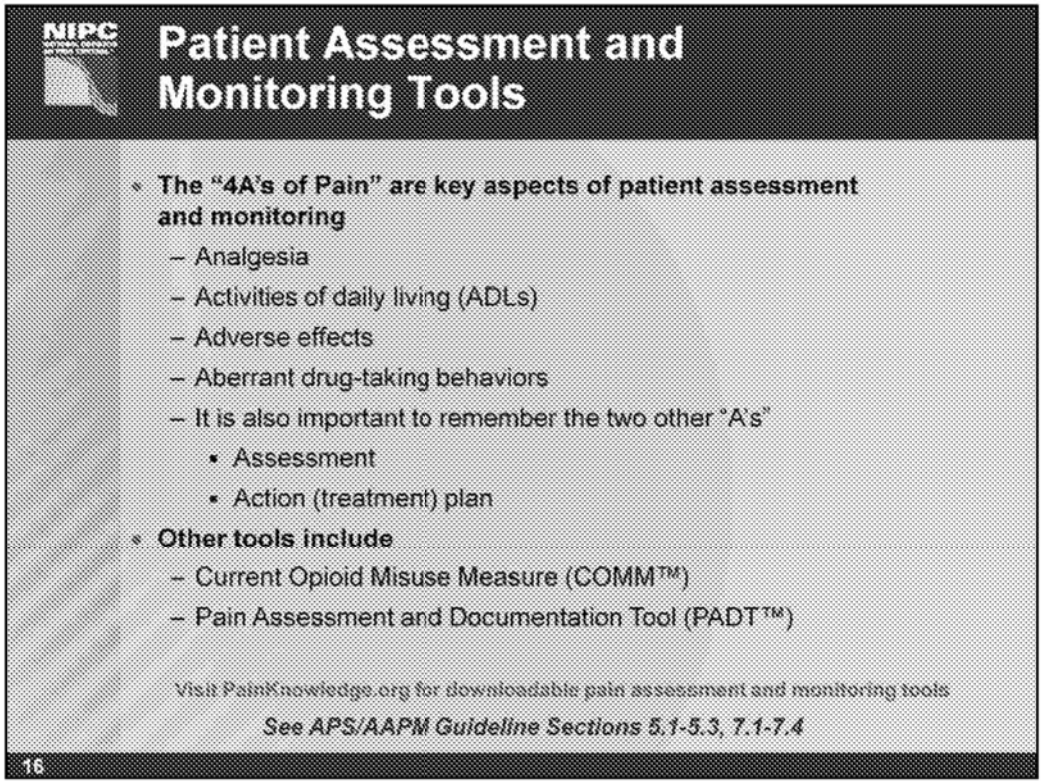
The "opioid therapy patient agreement" has been developed to help address some of these issues and concerns. Opioid agreements are intended to improve adherence to therapy and to enhance therapeutic relationships by initiating an alliance between the patient and the physician.

Opioid agreements may vary distinctly in tone and demeanor. The language in which some agreements are couched is designed to invoke a sense of cooperation and equality. These agreements often devote considerable space to explanations of their utility and value. They stress the rights and responsibilities of both the healthcare provider and the patient. They offer broad, generalized, and nonconfrontational guidelines and avoid proscriptions or commandments. Other agreements are more dogmatic in tone. Their language is more authoritative, more concerned with the presentation of detailed rules and procedures. These agreements tend to outline specific consequences for breaking the agreement, and usually contain less in the way of educational information.

Each type of agreements offers advantages and each may entail certain disadvantages. The more equitable, less confrontational agreements enable patients to feel they are taking a more active role in their therapy—the sort of perception that may serve to improve compliance. On the other hand, the broader, less explicit language featured in these agreements might decrease compliance—because the patient has not been given strict, unambiguous rules to follow.

The more dogmatic, rule-giving agreements may have the advantage of laying down very clear guidelines, but they may make the patient feel he or she is not trusted, or is not being treated as a rational, decision-making adult. Such agreements may also unwittingly stigmatize opioids by fostering the impression that opioid use is bad or dangerous.

Fishman SM, Bandman BA, Edwards A, Borsook D. The opioid contract. *J Pain Symptom Manage*. 1999;18:27-37

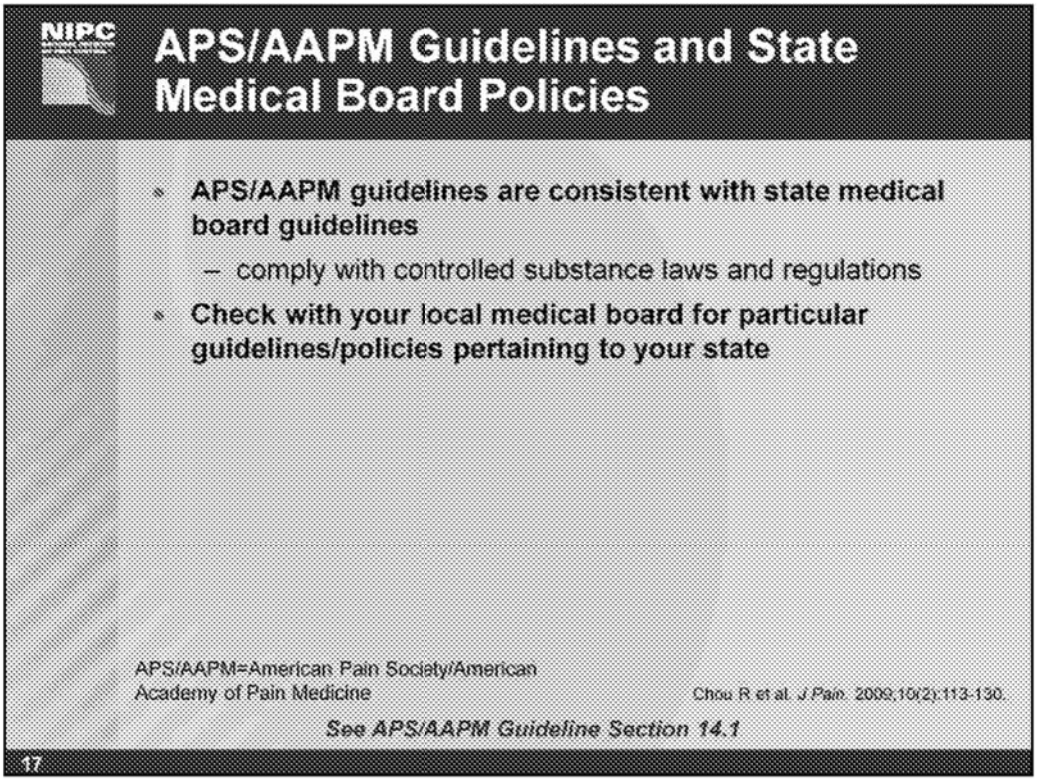


The "Four A's of Pain" outcome assessment provides a useful approach for the physician to appropriate follow-up for guiding optimal pain management.

Key points include the importance of monitoring patients' pain intensity to ensure that they are receiving effective analgesia (pain relief), measuring effects on activities of daily living to document improvements in patient physical and psychosocial functioning, and closely monitoring for adverse effects (side effects) in order to minimize or counter these effects, and being vigilant for any signs of aberrant drug-taking behaviors that may precede addiction or addiction-related behaviors.

Assessment and treatment documentation should include justification for continuing, modifying, or discontinuing opioid analgesia.

Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. *Adv Ther.* 2000;17:70-83.



Federation of State Medical Boards of the United States, Inc. Model Policy for the Use of Controlled Substances for the Treatment of Pain. Available at: http://www.painpolicy.wisc.edu/domestic/model04.pdf

NIPC

Meet Mr Smith, Dr Brown's Patient

- **60-year-old man who recently arrived from another state presents with low back pain (LBP)/bone pain of 6 months' duration, well controlled on methadone 20 mg tid**
- **Medical records brought with him indicate**
  - inoperable prostate cancer previously treated with radiation
    - currently on hormone suppression therapy
  - metastases to the lumbar spine indicated by previous physician as cause of LBP
    - has failed bisphosphonates (zoledronic acid), radiopharmaceuticals (strontium-89), and interventional measures for control of LBP/bone pain before current opioid regimen

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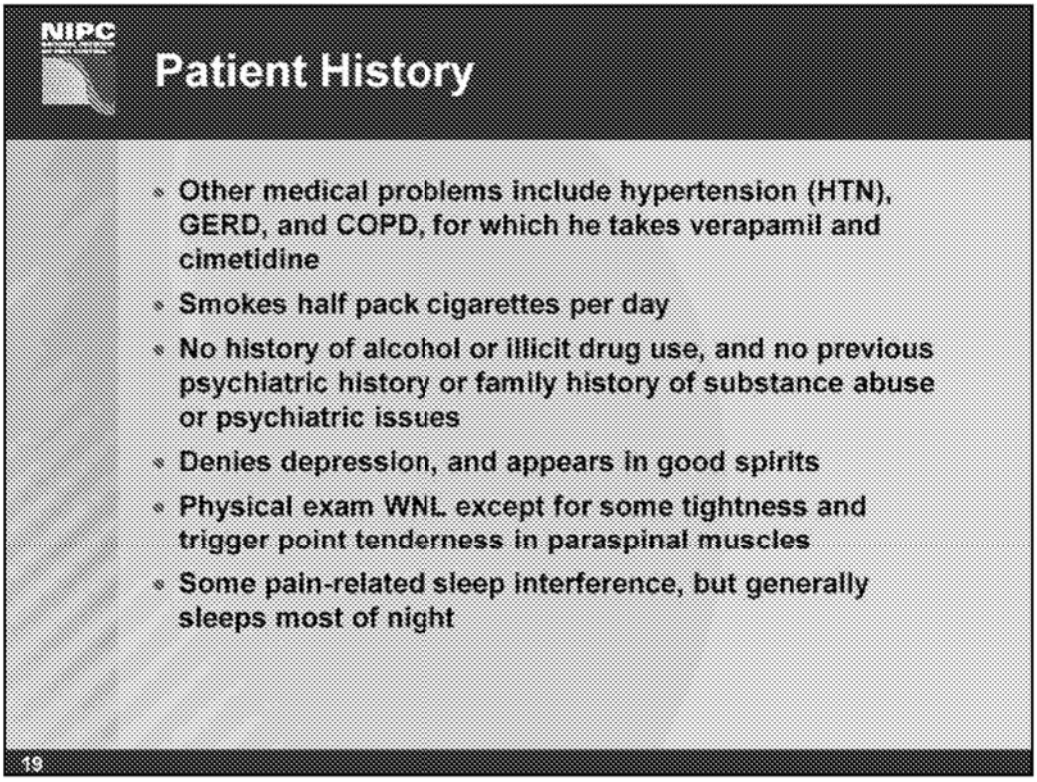
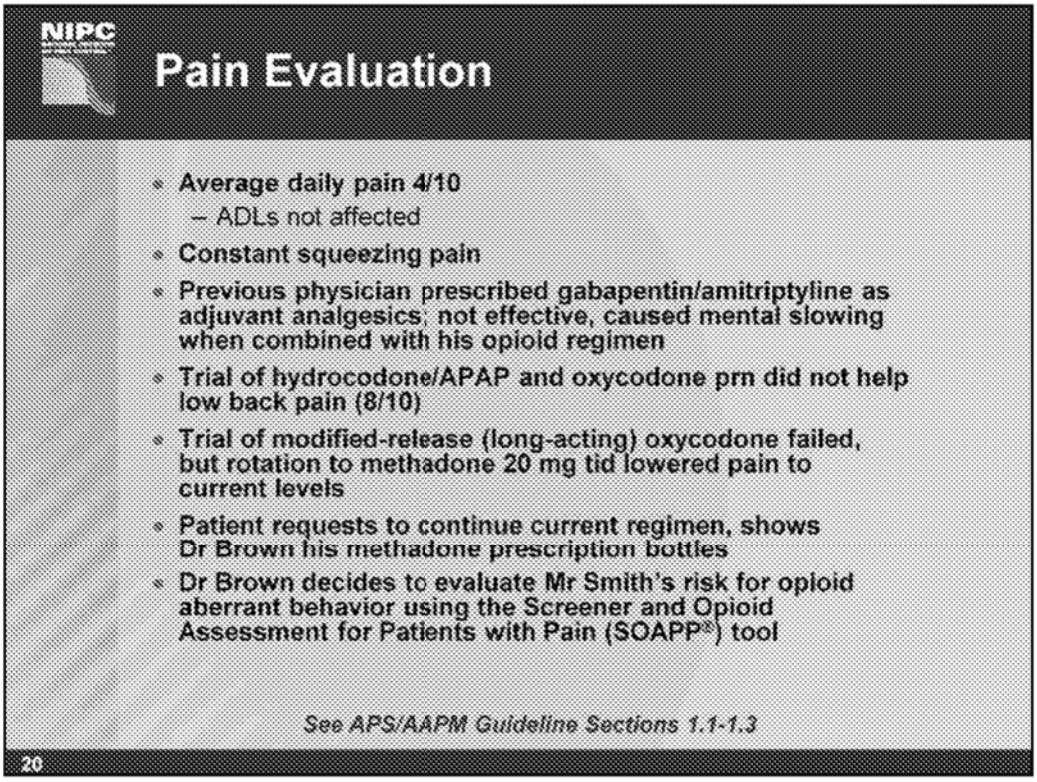
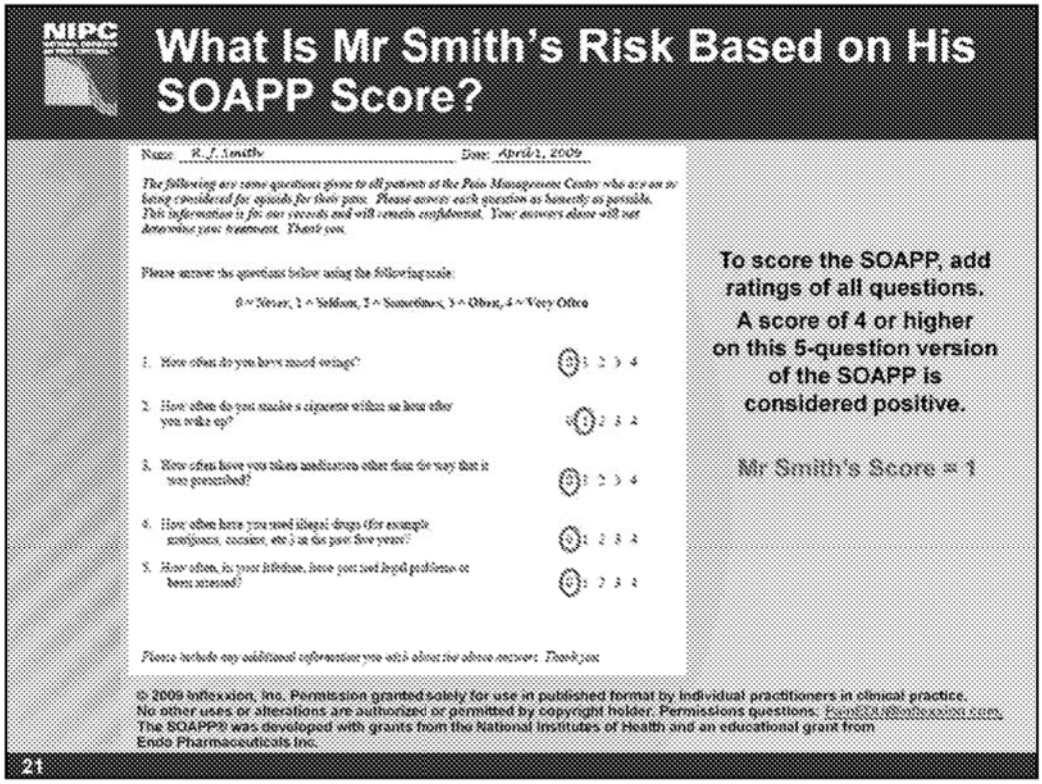

NIPC
Patient History
Other medical problems include hypertension (HTN), GERD, and COPD, for which he takes verapamil and cimetidine
Smokes half pack cigarettes per day
No history of alcohol or illicit drug use, and no previous psychiatric history or family history of substance abuse or psychiatric issues
Denies depression, and appears in good spirits
Physical exam WNL except for some tightness and trigger point tenderness in paraspinal muscles
Some pain-related sleep interference, but generally sleeps most of night
19


NIPC
Pain Evaluation
Average daily pain 4/10
– ADLs not affected
Constant squeezing pain
Previous physician prescribed gabapentin/amitriptyline as adjuvant analgesics; not effective, caused mental slowing when combined with his opioid regimen
Trial of hydrocodone/APAP and oxycodone prn did not help low back pain (8/10)
Trial of modified-release (long-acting) oxycodone failed, but rotation to methadone 20 mg tid lowered pain to current levels
Patient requests to continue current regimen, shows Dr Brown his methadone prescription bottles
Dr Brown decides to evaluate Mr Smith's risk for opioid aberrant behavior using the Screener and Opioid Assessment for Patients with Pain (SOAPP®) tool
See APS/AAPM Guideline Sections 1.1-1.3
20

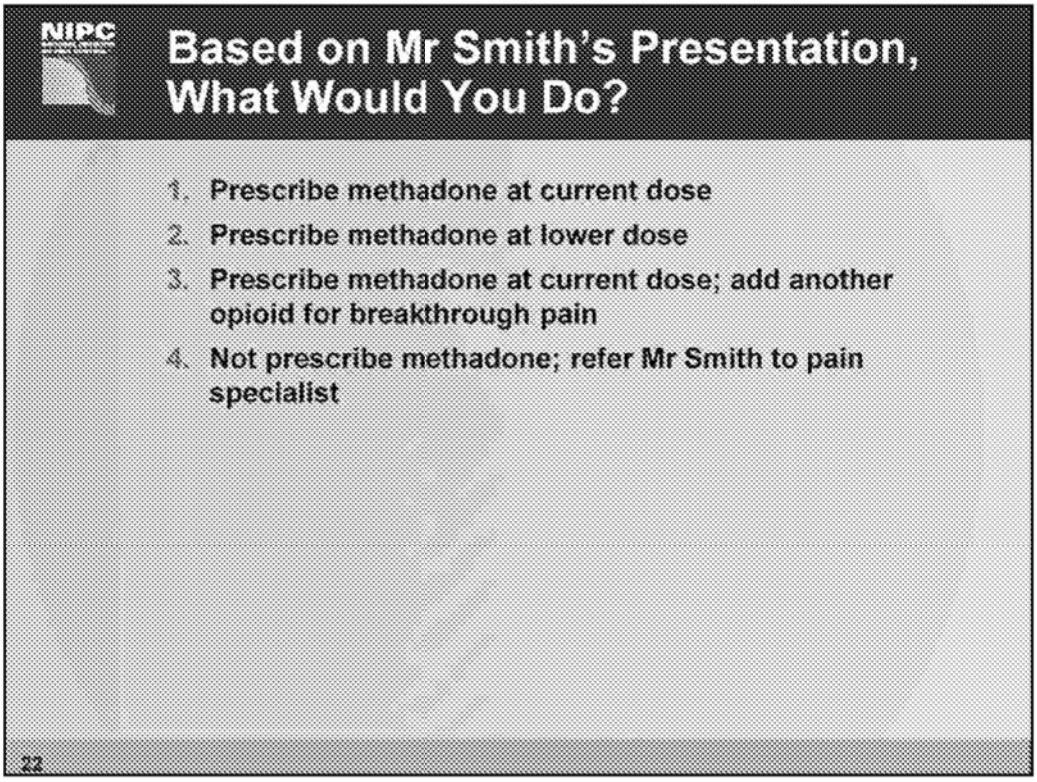


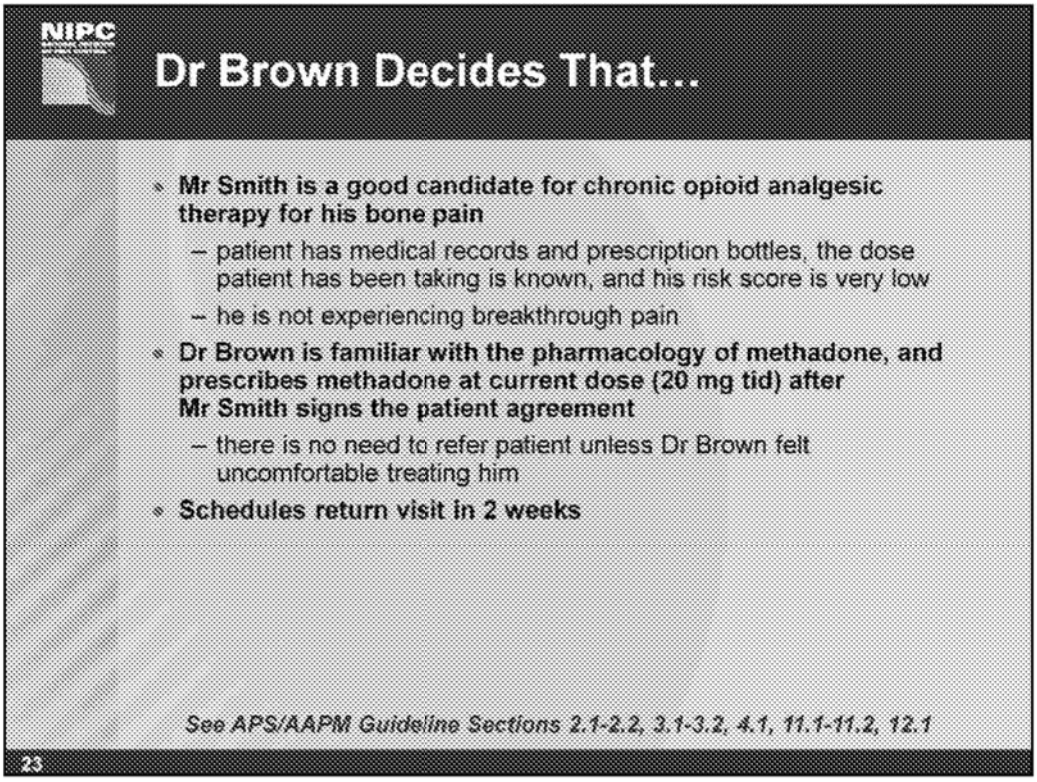
The five questions that make up the SOAPP V.1-SF have been empirically identified as predicting aberrant medication-related behavior six months after initial testing.

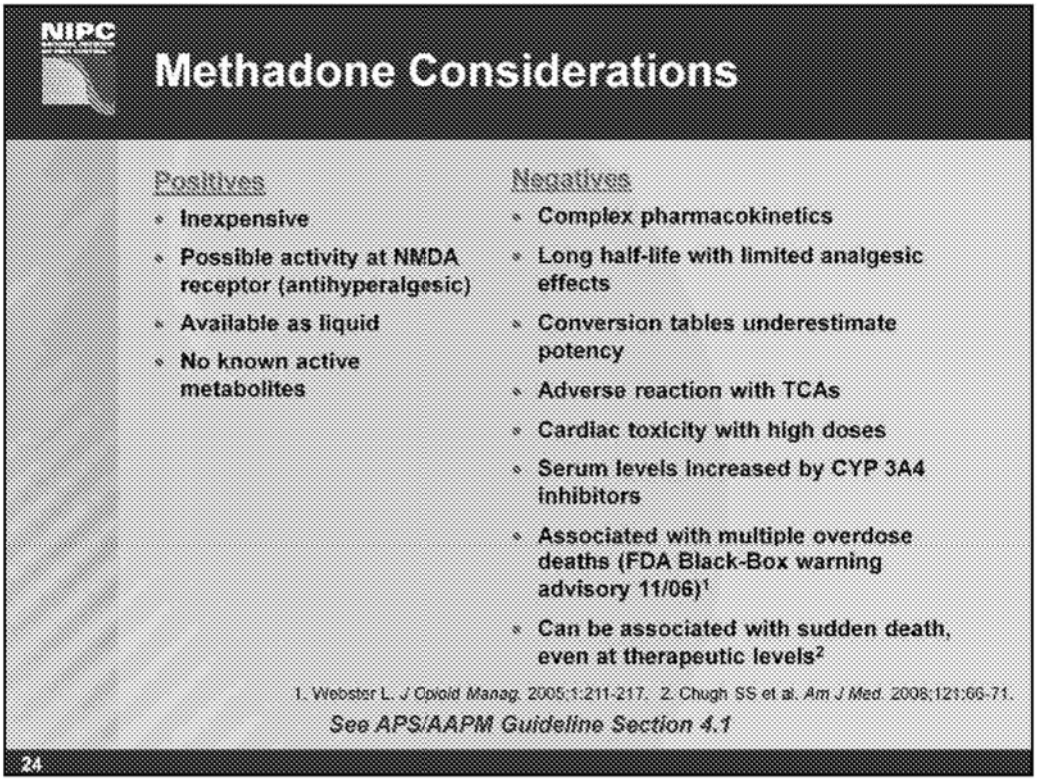
What does the Short Form Cutoff Score Mean?

In general, there is a trade off between the length of a questionnaire and its accuracy as a screener. Thus, to achieve a shorter form, one must live with poorer sensitivity and specificity. Naturally, the question becomes, "how much accuracy is traded for a shorter form?" In comparing the Standard 14-item statistics with those of the SOAPP V.1-SF, in our view, while these parameters are clearly not as good as for the full 14-item scoring, the reduction in sensitivity, specificity, positive and negative predictive values and likelihood ratios suggests that the five-item version retains most of the predictive validity of the Standard SOAPP version. As with any screener, the scores above a cutoff will necessarily include a number of patients that are not really at risk. Scores below the cutoff will, in turn, miss a number of patients at risk. A screening measure like the SOAPP generally endeavors to minimize the chances of missing high-risk patients. This means that patients who are truly at low risk may still get a score above the cutoff. When comparing the values for both versions, the data shows that the SOAPP short form, like the Standard SOAPP, is a sensitive test. This confirms that the SOAPP is better at identifying who is at high risk than identifying who is at low risk. Clinically, a score of 4 or higher will identify 86% of those who actually turn out to be at high risk (compared to 91% for the 14-item version). The Negative Predictive Values for a cutoff score of 4 is .85, which means that most people who have a negative SOAPP are likely at low-risk. Finally, the Positive likelihood ratio suggests that a positive SOAPP score (at a cutoff of 4) is more than two and half times (2.59 times) as likely to come from

someone who is actually at high risk (compare with 2.94 for the Standard SOAPP). Note that, of these statistics, the likelihood ratio is least affected by prevalence rates. All this implies that by using a cutoff score of 4will ensure that the provider is least likely to miss someone who is really at high risk. However, one should remember that a low SOAPP score suggests the patient is really at low-risk, while a high SOAPP score will contain a larger percentage of false positives (about 33%), while at the same time retaining a large percentage of true positives. The SOAPP is less good at identifying who is not at-risk. Thus, the SOAPP V1-SF appears to strike a reasonable balance between length and ability to detect future aberrant behavior.


NIPC
Based on Mr Smith's Presentation, What Would You Do?
1. Prescribe methadone at current dose
2. Prescribe methadone at lower dose
3. Prescribe methadone at current dose; add another opioid for breakthrough pain
4. Not prescribe methadone; refer Mr Smith to pain specialist
22


NIPC
Dr Brown Decides That...
Mr Smith is a good candidate for chronic opioid analgesic therapy for his bone pain
– patient has medical records and prescription bottles, the dose patient has been taking is known, and his risk score is very low
– he is not experiencing breakthrough pain
Dr Brown is familiar with the pharmacology of methadone, and prescribes methadone at current dose (20 mg tid) after Mr Smith signs the patient agreement
– there is no need to refer patient unless Dr Brown felt uncomfortable treating him
Schedules return visit in 2 weeks
See APS/AAPM Guideline Sections 2.1-2.2, 3.1-3.2, 4.1, 11.1-11.2, 12.1
23



Webster L. Methadone-related deaths. *J Opioid Manag*. 2005;1(4):211-217.

Chugh SS, Socoteanu C, Reinier K, Waltz J, Jui J, Gunson K. A community-based evaluation of sudden death associated with therapeutic levels of methadone. *Am J Med*. 2008;121(1):66-71.

NIPC

Mr Smith: Follow-up Visit in 2 Weeks

"A's" Reassessment Chart Note

- Analgesia: **Reports good pain relief**
  - average pain intensity → 3-4/10
- AEs: **None**
- ADLs: **Function → same, but now complains of severe sleep difficulties (waking up 3-4x/night), not related to pain. Also complains of excessive daytime drowsiness**
- Aberrant Drug-Taking Behavior: **None; taking meds as prescribed**
- Assessment Impression: **Good pain control on current dose; sleeping problems**
- Action Plan: **What would you do now?**

See APS/AAPM Guideline Sections 2.1-2.2, 5.1-5.3, 6.1-6.2, 8.1

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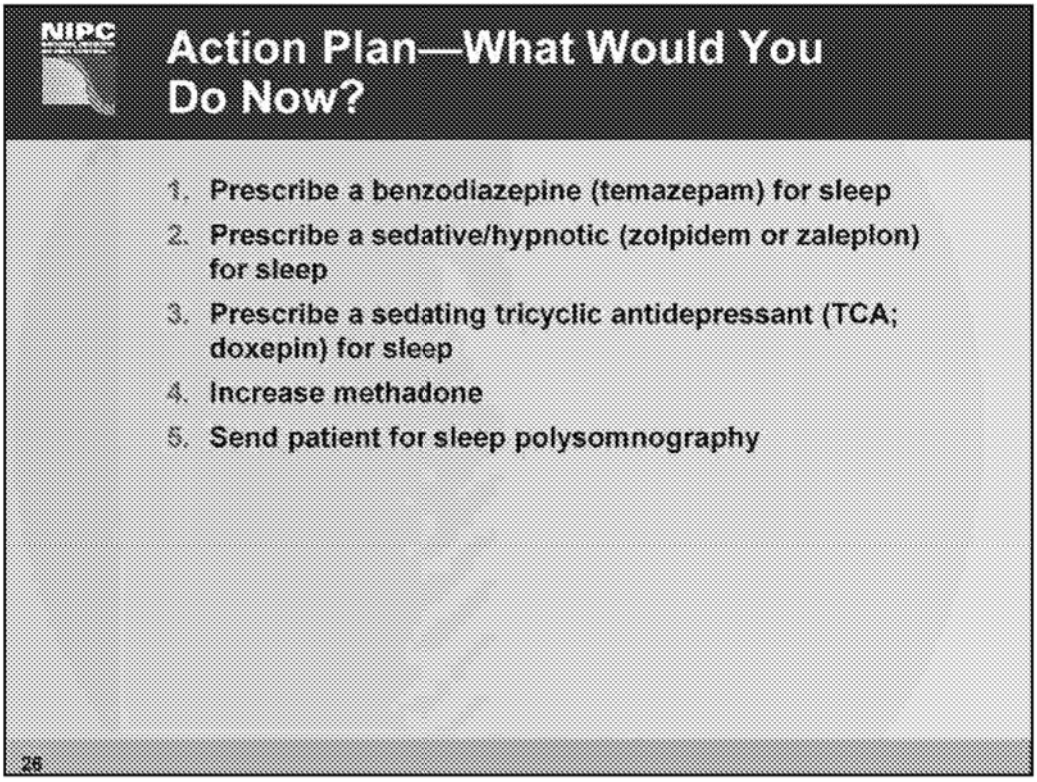
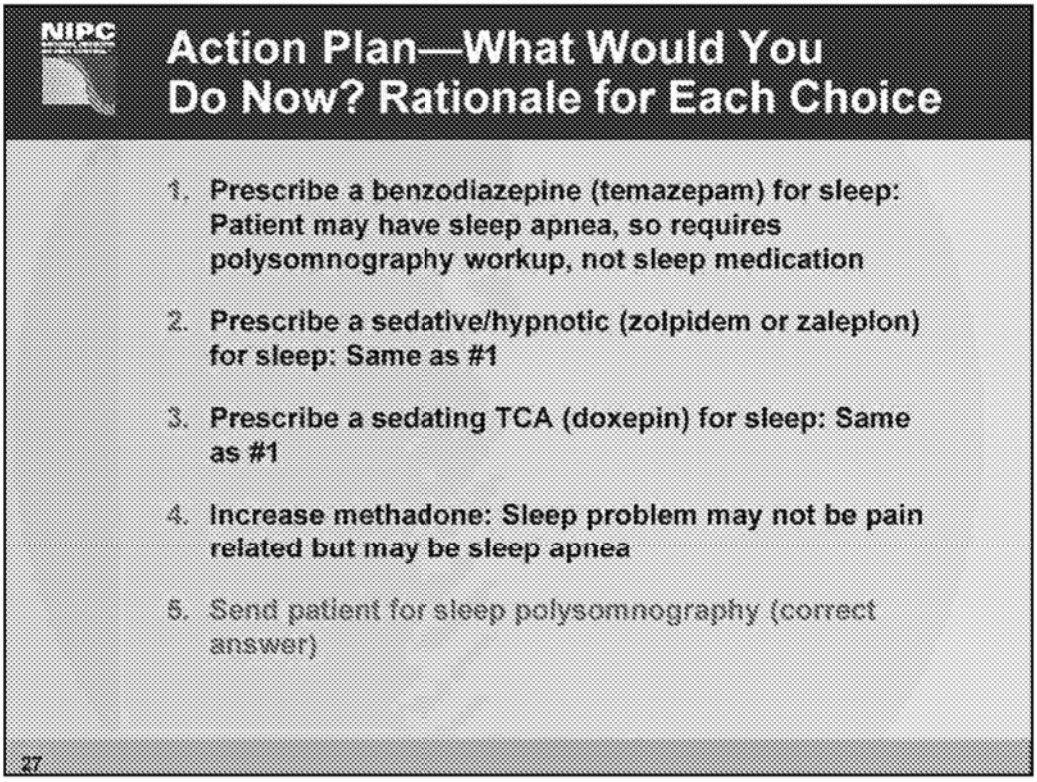
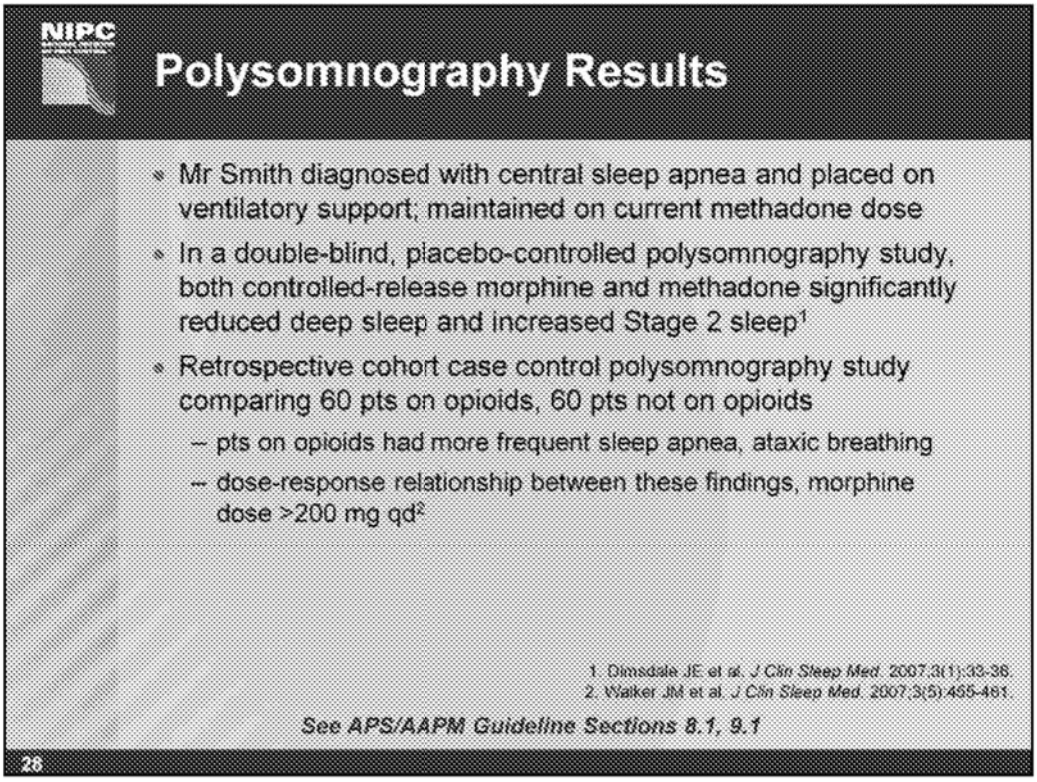

NIPC
Action Plan—What Would You Do Now?
1. Prescribe a benzodiazepine (temazepam) for sleep
2. Prescribe a sedative/hypnotic (zolpidem or zaleplon) for sleep
3. Prescribe a sedating tricyclic antidepressant (TCA; doxepin) for sleep
4. Increase methadone
5. Send patient for sleep polysomnography
28


NIPC
Action Plan—What Would You Do Now? Rationale for Each Choice
1. Prescribe a benzodiazepine (temazepam) for sleep: Patient may have sleep apnea, so requires polysomnography workup, not sleep medication
2. Prescribe a sedative/hypnotic (zolpidem or zaleplon) for sleep: Same as #1
3. Prescribe a sedating TCA (doxepin) for sleep: Same as #1
4. Increase methadone: Sleep problem may not be pain related but may be sleep apnea
5. Send patient for sleep polysomnography (correct answer)
27



Wang D, Teichtahl H, Drummer O, Goodman C, Cherry G, Cunnington D, Kronborg I. Central sleep apnea in stable methadone maintenance treatment patients. *Chest*. 2005;128(3):1348-1356.

Teichtahl H, Prodromidis A, Miller B, Cherry G, Kronborg I. Sleep-disordered breathing in stable methadone programme patients: a pilot study. *Addiction*. 2001;96(3):395-403.

Webster LR, Choi Y, Desai H, Grant BJB, Webster L. Sleep-disordered breathing and chronic opioid therapy. *Pain Med*. Published article online: 30-Jul-2007. doi: 10.1111/j.1526-4637.2007.00343.x.

Dimsdale JE, Norman D, DeJardin D, Wallace MS. The effect of opioids on sleep architecture. *J Clin Sleep Med*. 2007;3(1):33-36.

Walker JM, Farney RJ, Rhondeau SM, Boyle KM, Valentine K, Cloward TV, Shilling KC. Chronic opioid use is a risk factor for the development of central sleep apnea and ataxic breathing. *J Clin Sleep Med*. 2007;3(5):455-461.

NIPC

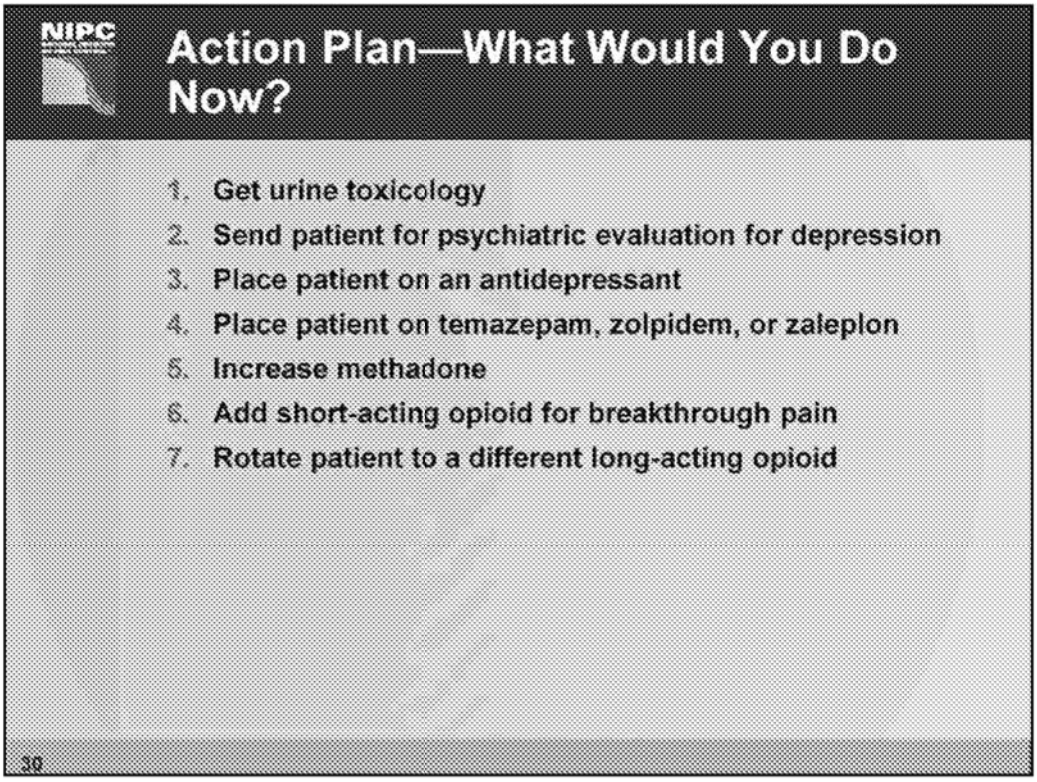
Follow-up Visit 2 Weeks Early

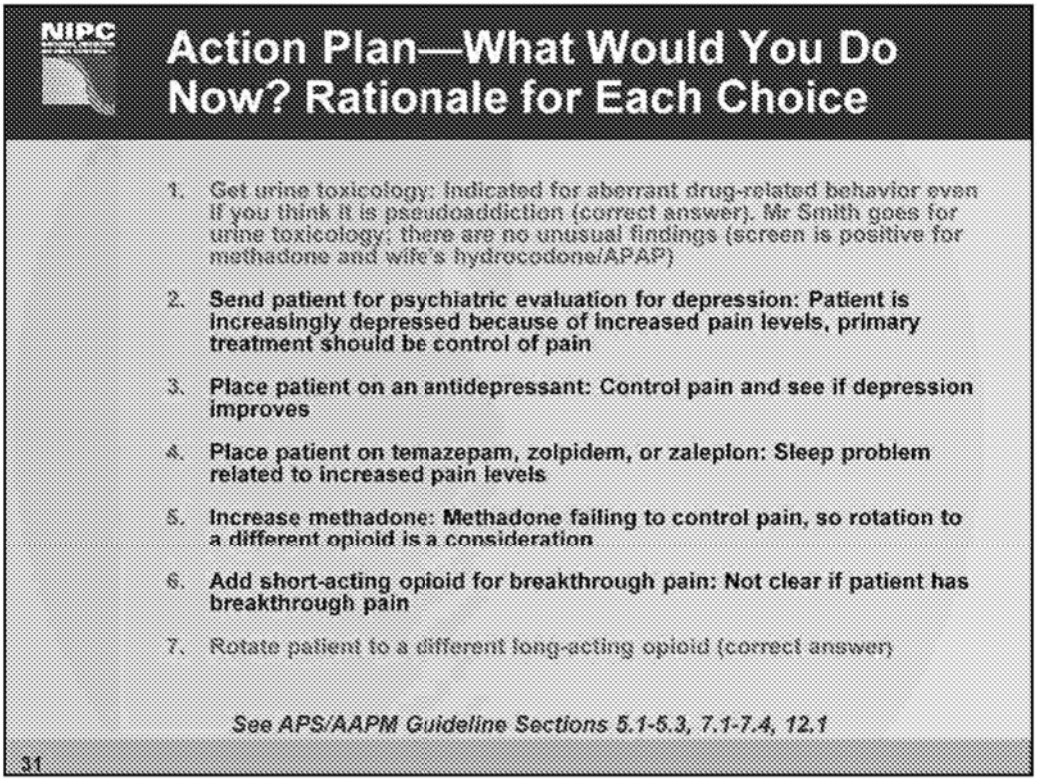
"A's" Reassessment Chart Note

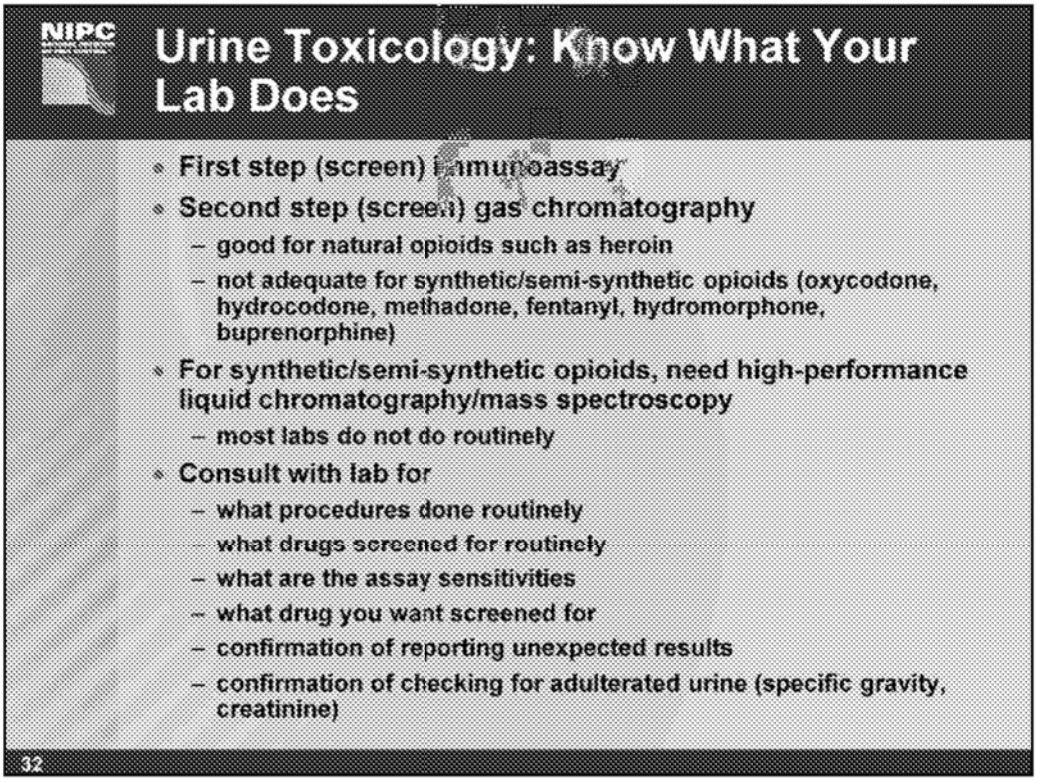
- Analgesia: **Patient reports progressive increase in pain to 7/10 with little relief from the methadone; patient states that he does not wish to live like this and that nothing is working. "It's time to face reality and go quietly"**
- AEs: **None**
- ADLs: **Function now severely impaired with sleep worse, even with ventilatory support**
- Aberrant Drug-Taking Behavior: **Spouse reports patient taking her hydrocodone/APAP in addition to his methadone to control pain**
- Assessment Impression: **Disease progression with increased pain, and aberrant drug-related behavior**
- Action Plan: **What would you do now?**

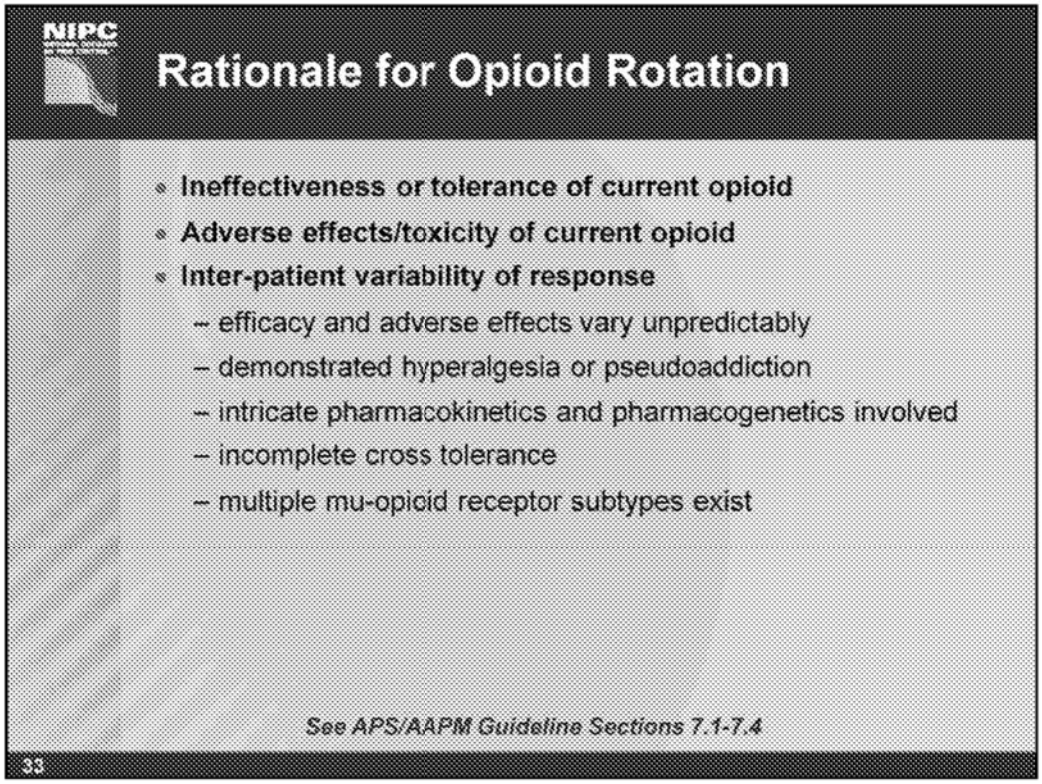
See APS/AAPM Guideline Sections 2.1-2.2, 6.1-6.2

29


NIPC
Action Plan—What Would You Do Now?
1. Get urine toxicology
2. Send patient for psychiatric evaluation for depression
3. Place patient on an antidepressant
4. Place patient on temazepam, zolpidem, or zaleplon
5. Increase methadone
6. Add short-acting opioid for breakthrough pain
7. Rotate patient to a different long-acting opioid
30


NIPC
Action Plan—What Would You Do Now? Rationale for Each Choice
1. Get urine toxicology: Indicated for aberrant drug-related behavior even if you think it is pseudoaddiction (correct answer). Mr Smith goes for urine toxicology; there are no unusual findings (screen is positive for methadone and wife's hydrocodone/APAP)
2. Send patient for psychiatric evaluation for depression: Patient is increasingly depressed because of increased pain levels, primary treatment should be control of pain
3. Place patient on an antidepressant: Control pain and see if depression improves
4. Place patient on temazepam, zolpidem, or zaleplon: Sleep problem related to increased pain levels
5. Increase methadone: Methadone failing to control pain, so rotation to a different opioid is a consideration
6. Add short-acting opioid for breakthrough pain: Not clear if patient has breakthrough pain
7. Rotate patient to a different long-acting opioid (correct answer)
See APS/AAPM Guideline Sections 5.1-5.3, 7.1-7.4, 12.1
31


NIPC
Urine Toxicology: Know What Your Lab Does
First step (screen) immunoassay
Second step (screen) gas chromatography
good for natural opioids such as heroin
not adequate for synthetic/semi-synthetic opioids (oxycodone, hydrocodone, methadone, fentanyl, hydromorphone, buprenorphine)
For synthetic/semi-synthetic opioids, need high-performance liquid chromatography/mass spectroscopy
most labs do not do routinely
Consult with lab for
what procedures done routinely
what drugs screened for routinely
what are the assay sensitivities
what drug you want screened for
confirmation of reporting unexpected results
confirmation of checking for adulterated urine (specific gravity, creatinine)
32



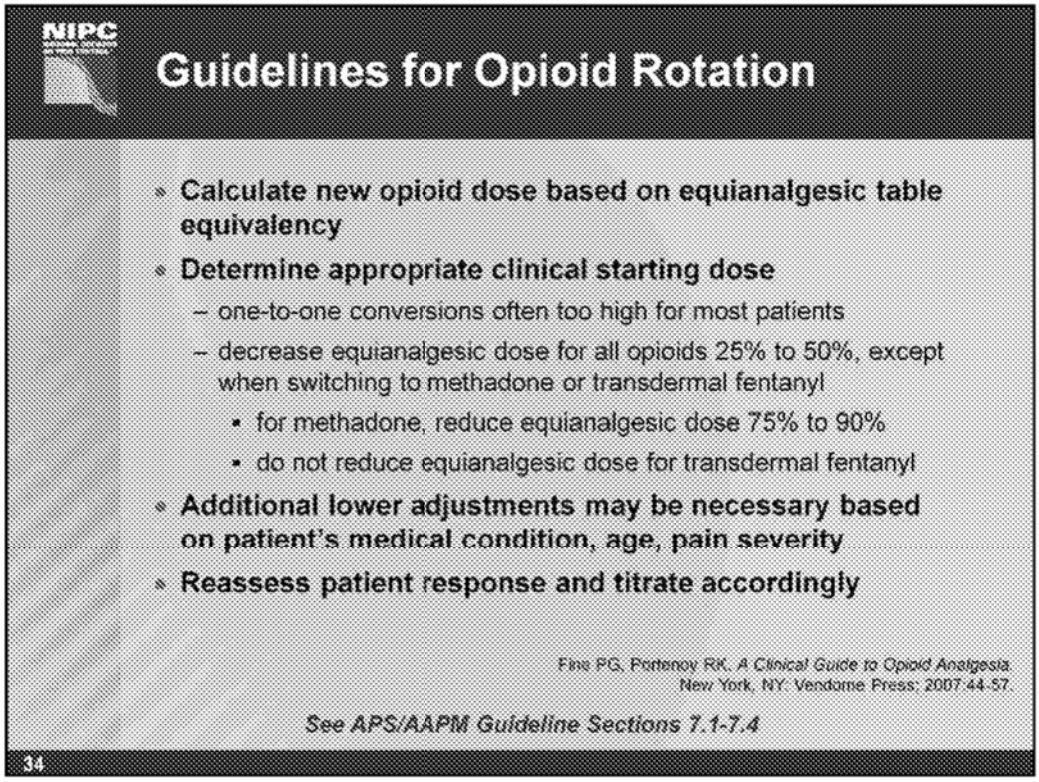
In their trial of opioids for rheumatologic nonmalignant pain, Grilo et al enrolled 67 patients in whom other analgesics had failed.[1] The opioids used were oral morphine, oral hydromorphone, oral buprenorphine, and transdermal fentanyl. The 67 patients suffered from low back pain with sciatica in 27 cases, inflammatory arthritis in 14 cases, brachial neuralgia in 6 cases, osteoarthritis in 8 cases, and miscellaneous conditions in 12 cases. The opioid rotations in most of the cases were the substitution of morphine by transdermal fentanyl or by oral hydromorphone. The principal reason for opioid rotation was failure of the first treatment. The mean of visual analog scale (VAS) improvement was 30 mm (P<.001). The authors concluded that in rheumatologic nonmalignant pain, the opioid rotation might allow the physician to bypass side effects or failure to alleviate pain in most cases.

In their retrospective chart review, Quang-Cantagrel et al found that the first opioid prescribed was effective for 36% of patients, was stopped because of side effects in 30%, and was stopped for ineffectiveness in 34%.[2] Of the remaining patients, the second opioid prescribed after the failure of the first was effective in 31%, the third in 40%, the fourth in 56%, and the fifth in 14%. There was one case of addiction and no cases of tolerance. The authors concluded that if it is necessary to change the opioid prescription because of intolerable side effects or ineffectiveness, the cumulative percentage of efficacy increases with each new opioid tested. Failure of one opioid cannot predict the patient's response to another.[3]

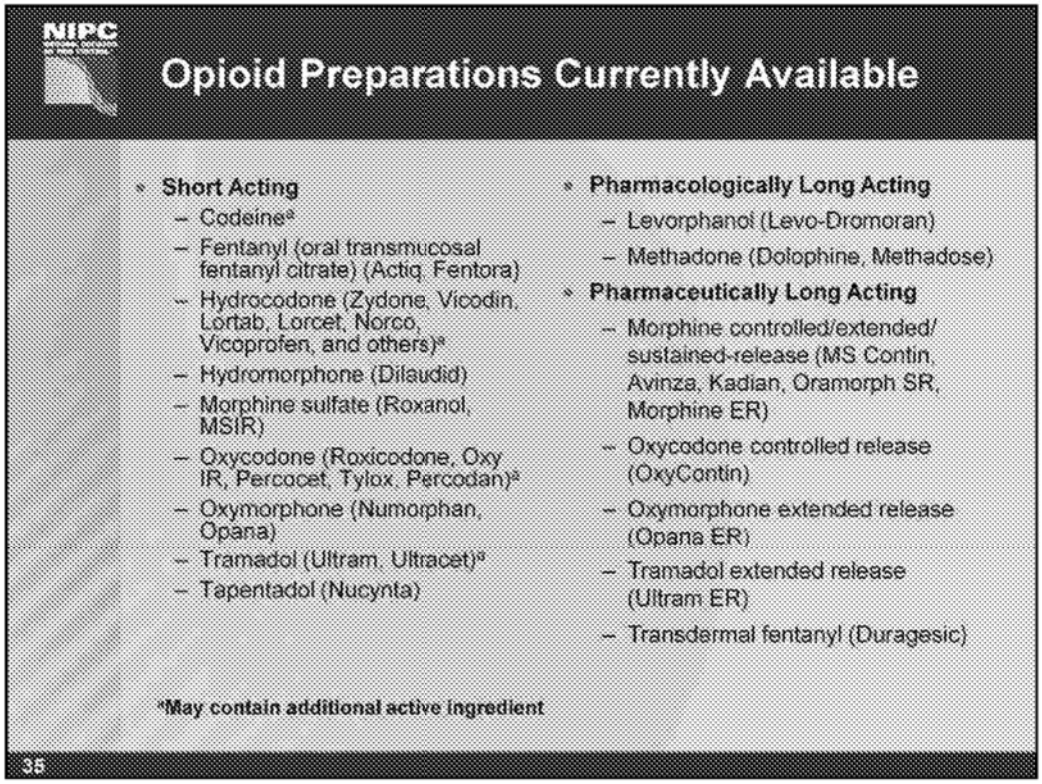
1. Grilo RM, Bertin P, Scotto di Fazano C, et al. Opioid rotation in the treatment of joint pain: a review of 67 cases. *Joint Bone Spine*. 2002;69:491-494.

2. Quang-Cantagrel ND, Wallace MS, Magnuson S. Opioid substitution to improve the effectiveness of chronic noncancer pain control: a chart review. *Anesth Analg*. 2000;90:933-937.

3. Simpson KH. Individual choice of opioids and formulations: strategies to achieve the optimum for the patient. *Clin Rheumatol*. 2002;21(suppl 1):S5-S8.



Fine PG, Portenoy RK. Initiating and optimizing opioid therapy. In: *A Clinical Guide to Opioid Analgesia*. New York, NY: Vendome Press; 2007.



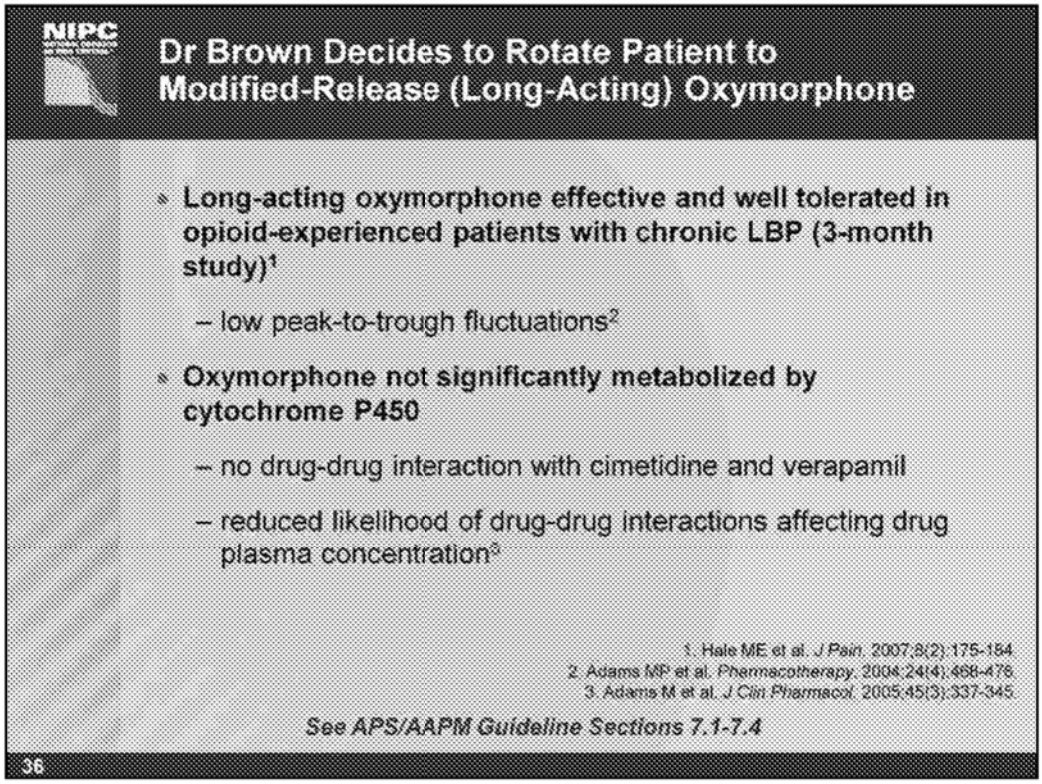
Short-acting opioids are appropriate for treatment of acute pain or breakthrough/incident pain, whereas long-acting formulations are used for patients with continuous chronic pain. Short-acting agents provide effective analgesia for acute pain but should be avoided as primary analgesics for chronic pain management, eg, the short-acting opioid meperidine is inappropriate for chronic pain analgesia because of its conversion to the toxic metabolite normeperidine, which can cause seizures. Short-acting opioids may be used during the initial dose titration period of long-acting formulations and as rescue medication for episodes of breakthrough/incidence pain.[1,2]

Some short- and long-acting opioids may also contain other analgesics (eg, oxycodone/acetaminophen, hydrocodone/ibuprofen), and the recommended maximal limits of such agents should be considered.

1. American Geriatric Society. Clinical Practice Guidelines. The management of chronic pain in older persons. *J Am Geriatr Soc*. 1998;46:635-651.

2. McCarberg BH, Barkin RL. Long-acting opioids for chronic pain: pharmacotherapeutic

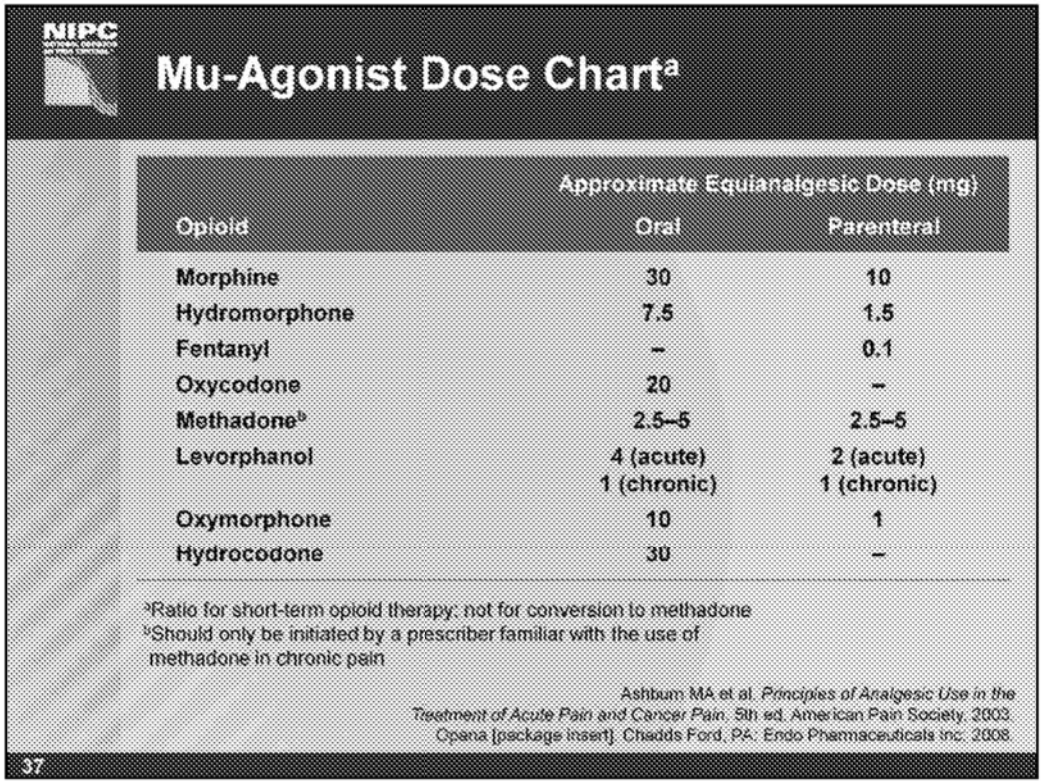
opportunities to enhance compliance, quality of life, and analgesia. *Am J Ther*. 2001;8:181-186.



Adams MP, Ahdieh H. Pharmacokinetics and dose-proportionality of oxymorphone extended release and its metabolites: results of a randomized crossover study. *Pharmacotherapy.* 2004 Apr;24(4):468-476.

Adams M, Pieniaszek HJ, Gammaitoni AR, Ahdieh H. Oxymorphone extended release does not affect CYP2C9 or CYP3A4 metabolic pathways. *J Clin Pharmacol.* 2005 Mar;45(3):337-45.

Hale ME, Ahdieh H, Ma T, Rauck R; the Oxymorphone ER Study Group 1. Efficacy and safety of OPANA ER (oxymorphone extended release) for relief of moderate to severe chronic low back pain in opioid-experienced patients: a 12-week, randomized, double-blind, placebo-controlled study. *J Pain.* 2007 Feb;8(2):175-184.



Mu-Agonist Dose Chart[a]

Opioid	Approximate Equianalgesic Dose (mg) Oral	Parenteral
Morphine	30	10
Hydromorphone	7.5	1.5
Fentanyl	–	0.1
Oxycodone	20	–
Methadone[b]	2.5–5	2.5–5
Levorphanol	4 (acute) 1 (chronic)	2 (acute) 1 (chronic)
Oxymorphone	10	1
Hydrocodone	30	–

[a]Ratio for short-term opioid therapy; not for conversion to methadone
[b]Should only be initiated by a prescriber familiar with the use of methadone in chronic pain

Ashburn MA et al. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 5th ed. American Pain Society; 2003.
Opana [package insert]. Chadds Ford, PA: Endo Pharmaceuticals Inc; 2008.

37

The clinical benefits of opioid rotation have focused attention on efficacy differences between opioids and their respective equianalgesic dose ratios.

Understanding the differences among opioids is critical to understanding their equianalgesic dose ratios and for adjusting therapy following rotation to a new analgesic.

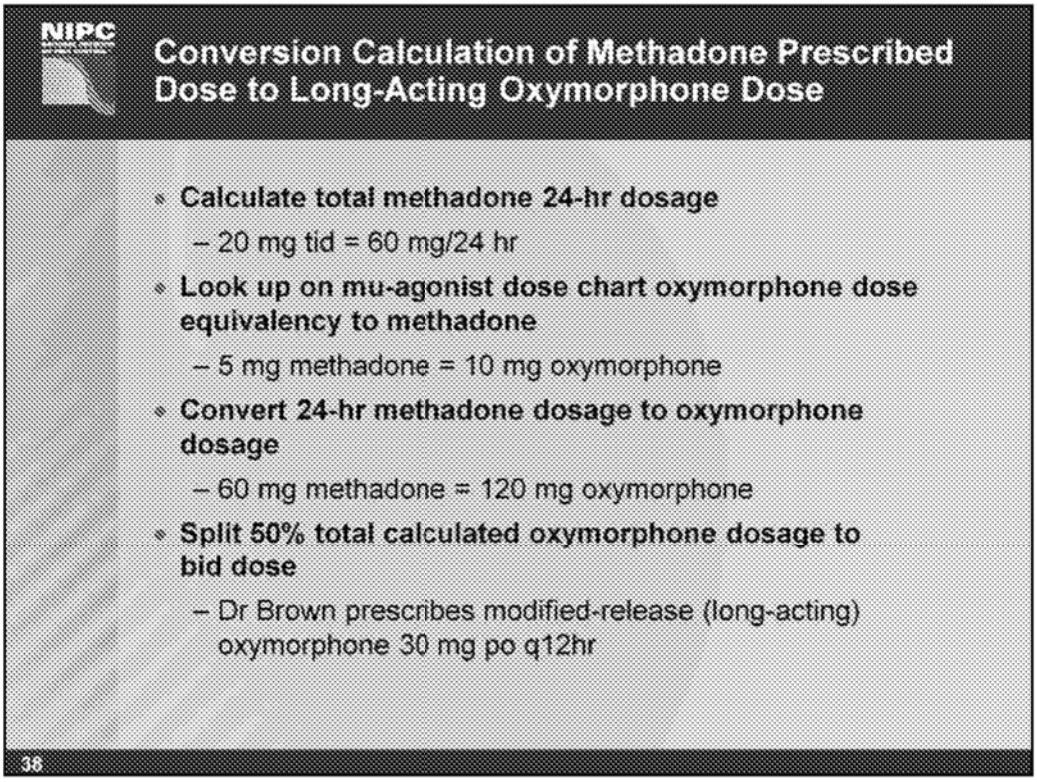
Dose ratios should be considered a guide. In particular, deviations from predicted doses may arise from incomplete cross tolerance, ie, patient may have become relatively tolerant to one opioid but have little tolerance to a new opioid. Incomplete cross tolerance is not possible to predict and probably depends on genetic factors, disease states, and concomitant medications.

Although analgesic dose tables are generally used to determine new doses in cases where opioid type or route of administration require changing, the evidence to support the ratios indicated in equianalgesic tables largely refers to the single-dose administration.

The applicability of these ratios to the chronic pain setting needs investigation.

Because of methadone's long half-life (average 15-30 hours), with drug accumulation over several days, methadone needs to be administered with caution with long intervals between dose adjustments (5-7 days). There have been deaths reported with the use of methadone for chronic pain. Although details are often unclear, many of these deaths may be due to conversion of patients from other opioids to methadone. Methadone has been associated with QRS prolongation, which can lead to sudden cardiac death. If unfamiliar with the the use of methadone, it is advisable to seek consultation with a pain specialist, especially when considering prescribing more than low-dose methadone (20-30 mg/day).

Anderson R, Saiers JH, Abram S, Schlicht C. Accuracy in equianalgesic dosing: conversion dilemmas. *J Pain Symptom Manage*. 2001;21:397-406.
Ashburn MA, Lipman AG, Carr D, et al. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*, 5th ed. Glenview, Ill: American Pain Society; 2003.
Drug Facts and Comparisons. Ed 58. Narcotic Agonist Analgesics. Wolters Kluwer Health, St Louis, 2004, 902, 914.
Max MB, Payne R, Edwards WT, et al. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain, 4th ed. Glenview, IL: American Pain Society;1999.
National Cancer Institute. Pain (PDQ®)
http://www.cancer.gov/cancertopics/pdq/supportivecare/pain/healthprofessional. Up-dated March 13, 2008. Accessed January 9, 2004.
Opana [package insert]. Chadds Ford, Pa: Endo Pharmaceuticals Inc.; 2006.
Pereira J, Lawlor P, Vigano A, Dorgan M, Bruena E. Equianalgesic dose ratios for opioids: a critical review and proposals for long-term dosing. *J Pain Symptom Manage*. 2001;22:672-687.


NIPC
Conversion Calculation of Methadone Prescribed Dose to Long-Acting Oxymorphone Dose
Calculate total methadone 24-hr dosage
– 20 mg tid = 60 mg/24 hr
Look up on mu-agonist dose chart oxymorphone dose equivalency to methadone
– 5 mg methadone = 10 mg oxymorphone
Convert 24-hr methadone dosage to oxymorphone dosage
– 60 mg methadone = 120 mg oxymorphone
Split 50% total calculated oxymorphone dosage to bid dose
– Dr Brown prescribes modified-release (long-acting) oxymorphone 30 mg po q12hr
38

NIPC

Patient Visit 3 Days Later

"A's" Reassessment Chart Note

- Analgesia: Average pain over 24 hrs → 5/10
- AEs: None
- ADLs: Function → somewhat improved
  - sleep slightly improved; less drowsy during the day; less hopeless
- Aberrant Drug-Taking Behavior: None per family. Urine toxicology ordered during last visit showed no illicit drugs; positive for methadone and wife's hydrocodone/APAP
- Assessment Impression: Improved pain control within tolerable range; no requirement for psych consult
- Action Plan: Continue modified-release (long-acting) oxymorphone at 30 mg po q12hr; workup for disease progression; and monitor for continued ventilatory support

See APS/AAPM Guideline Sections 5.1-5.3

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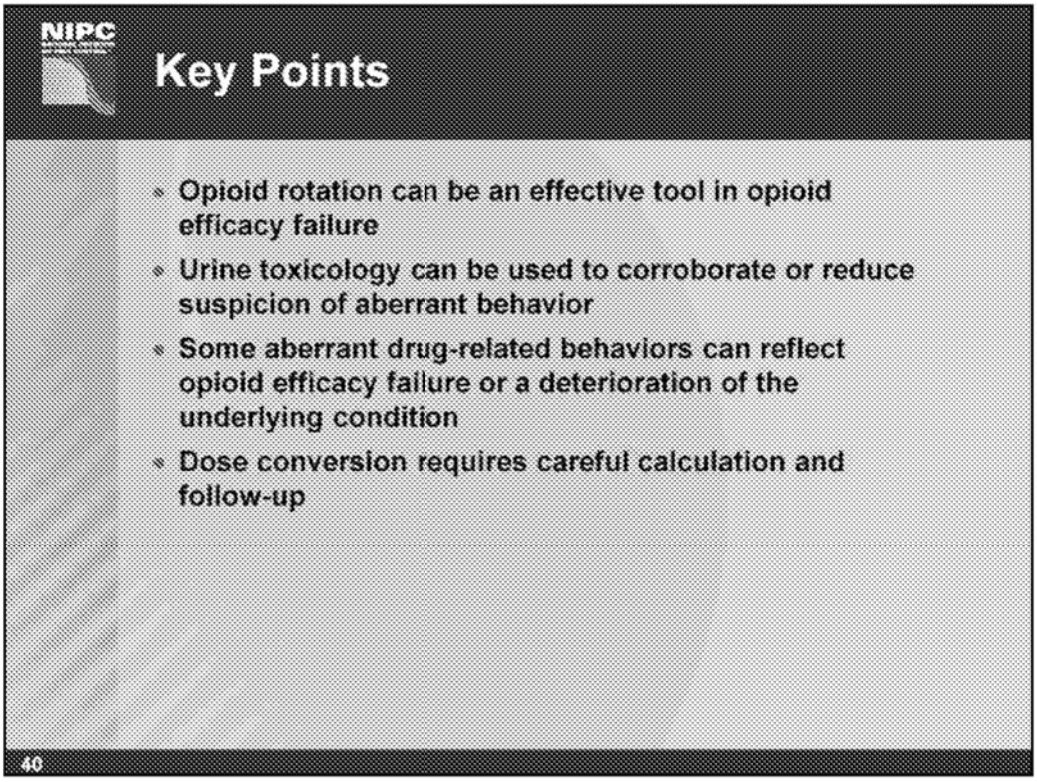
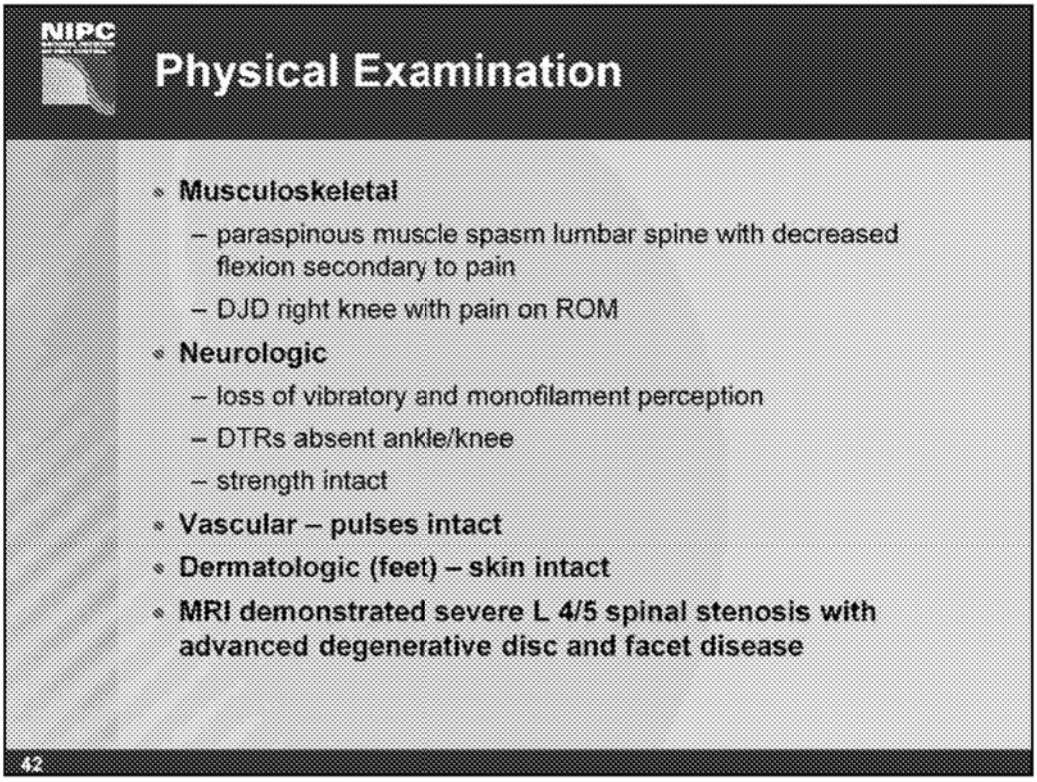

NIPC
Key Points
Opioid rotation can be an effective tool in opioid efficacy failure
Urine toxicology can be used to corroborate or reduce suspicion of aberrant behavior
Some aberrant drug-related behaviors can reflect opioid efficacy failure or a deterioration of the underlying condition
Dose conversion requires careful calculation and follow-up
40

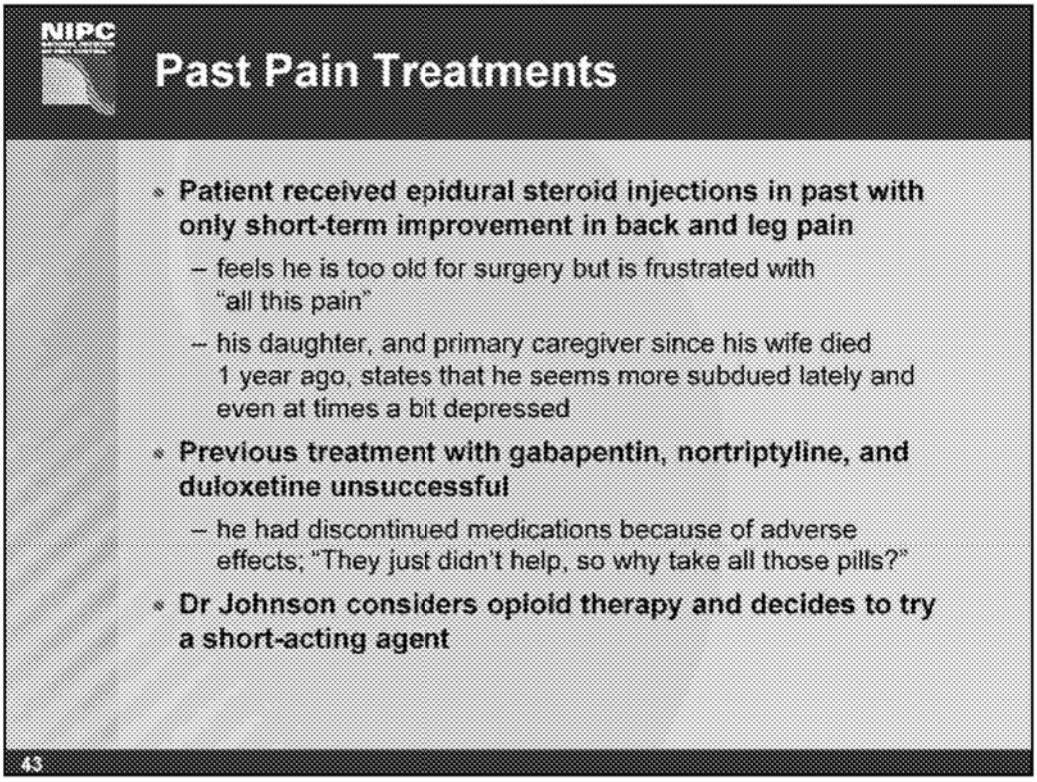
NIPC

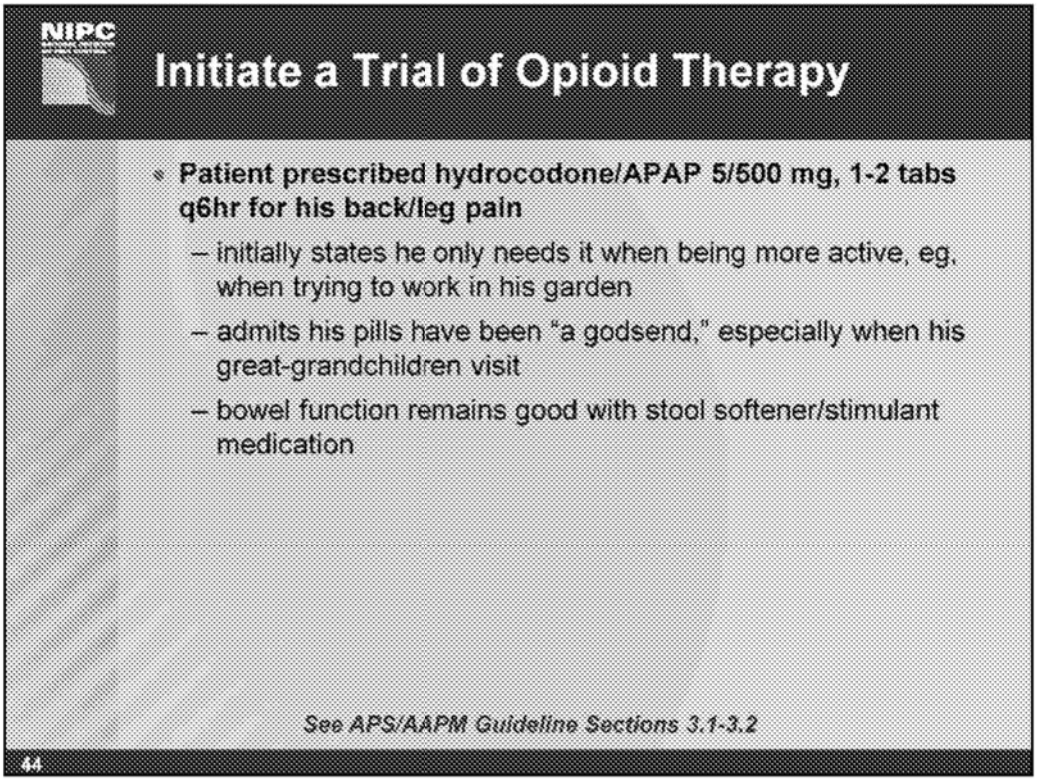
Meet Mr James, Dr Johnson's Patient

- **82-year-old man with LBP and leg pain gradually increasing during past 6 months**
  - pain worse with standing/walking and radiates down legs
  - back pain is 6/10 at rest and 8/10 with ambulation
  - leg pain is bilateral, gnawing, 8/10 with ambulation, and is relieved when he sits
- **Concurrent health problems**
  - type 2 diabetes, mild obesity
  - hyperlipidemia (metabolic syndrome)
  - HTN, osteoarthritis
- **Nonsmoker; no personal or family history of drug or alcohol abuse**
- **Current medications**
  - metformin
  - glipizide
  - "baby" aspirin
  - lisinopril
  - HCTZ
  - simvastatin
  - meloxicam

41


NIPC
Physical Examination
Musculoskeletal
– paraspinous muscle spasm lumbar spine with decreased flexion secondary to pain
– DJD right knee with pain on ROM
Neurologic
– loss of vibratory and monofilament perception
– DTRs absent ankle/knee
– strength intact
Vascular – pulses intact
Dermatologic (feet) – skin intact
MRI demonstrated severe L 4/5 spinal stenosis with advanced degenerative disc and facet disease
42


NIPC
Past Pain Treatments
Patient received epidural steroid injections in past with only short-term improvement in back and leg pain
– feels he is too old for surgery but is frustrated with "all this pain"
– his daughter, and primary caregiver since his wife died 1 year ago, states that he seems more subdued lately and even at times a bit depressed
Previous treatment with gabapentin, nortriptyline, and duloxetine unsuccessful
– he had discontinued medications because of adverse effects; "They just didn't help, so why take all those pills?"
Dr Johnson considers opioid therapy and decides to try a short-acting agent
43


NIPC
Initiate a Trial of Opioid Therapy
Patient prescribed hydrocodone/APAP 5/500 mg, 1-2 tabs q6hr for his back/leg pain
– initially states he only needs it when being more active, eg, when trying to work in his garden
– admits his pills have been "a godsend," especially when his great-grandchildren visit
– bowel function remains good with stool softener/stimulant medication
See APS/AAPM Guideline Sections 3.1-3.2
44

NIPC

Follow-up Visit 4 Months Later

"A's" Reassessment Chart Note

- Analgesia: Average pain slightly improved to 5/10 and 7/10 on ambulation
  - daughter thinks he has more pain than he admits; says he seems better for a short period of time, eg, 2-3 hours, when he takes his medication
- AEs: No bowel dysfunction, urinary retention, balance disturbance, cognitive impairment
- ADLs: Still not happy due to inability to work in garden; doesn't want the kids to visit that often
- Aberrant Drug-Taking Behavior: None
- Assessment Impression: May need around-the-clock (ATC) analgesia; Dr Johnson evaluates him with the SOAPP tool and he receives a score of 3
- Action Plan: Discuss ATC analgesia with patient and daughter; convert to a long-acting opioid

See APS/AAPM Guideline Sections 5.1-5.3, 12.1

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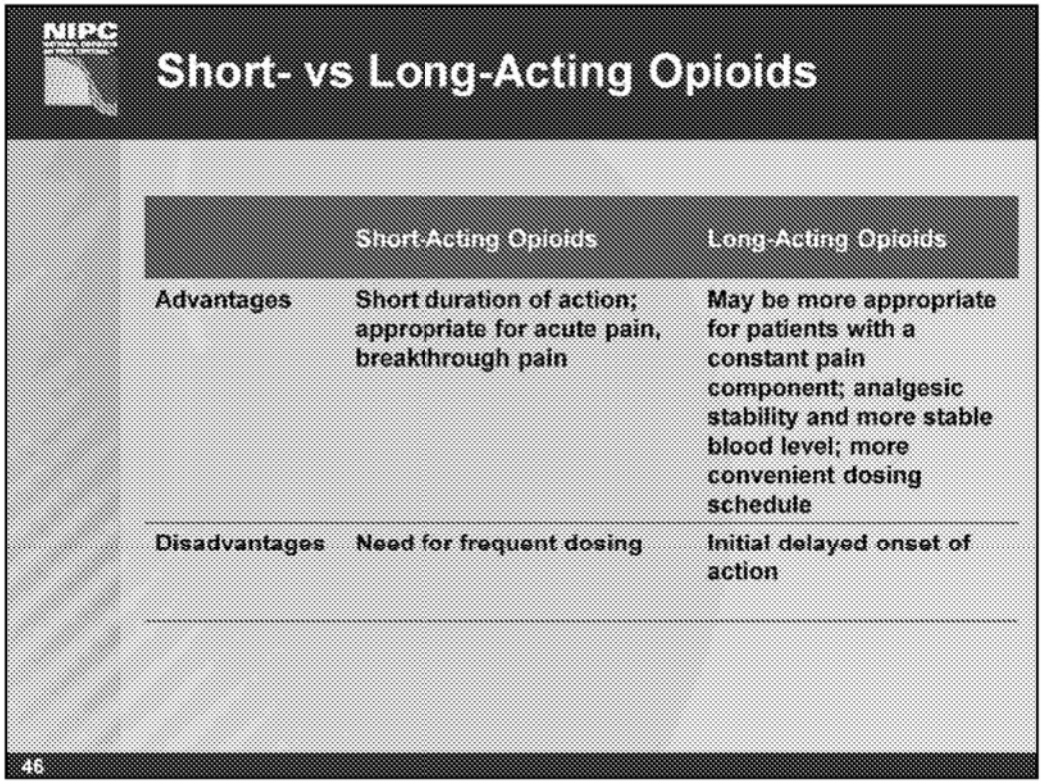


Thomsen et al note that during intervals between doses, patients treated with short-acting opioids may experience intermittent withdrawal symptoms, which may be misinterpreted as pain, or which may act to increase pain. Moreover a switch from short-acting opioids to long-acting opioids may reduce the pain-reinforcing properties of opioids, as a regularly scheduled opioid administration does not facilitate a behavior in which pain is rewarded with the administration of an opioid.

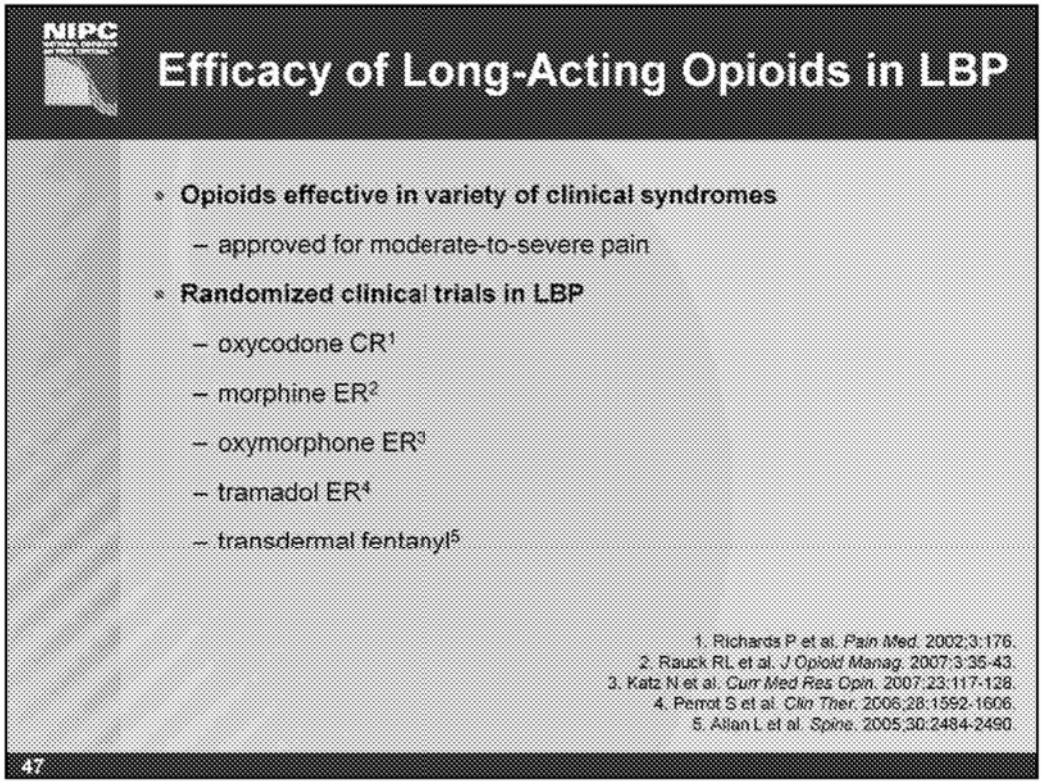
All of these disadvantages may be exacerbated in patients whose pain is chronic and intractable.

Although both short- and long-acting opioids have no ceiling effect, it may be more feasible to increase the dose (so as to increase the analgesia) of long-acting opioids (eg, methadone) because they tend to be less toxic than short-acting opioids (eg, morphine).

Repeated dosing of short-acting opioids may not provide the patient with optimal relief for chronic pain. Short-acting opioids often are administered in fixed combination with an acetaminophen or NSAID, imposing a ceiling effect on the maximum daily dose that can be administered. Long-acting agents invariably release the analgesics slowly, increase to therapeutic levels, plateau, and then decline in concentration. The long-acting opioids are better suited for moderate-to-severe pain because of their longer duration of action (typically 8 or 12 to 24 hours for oral formulations and up to 72 hours for transdermal fentanyl).

Glajchen M. Chronic pain: treatment barriers and strategies for clinical practice. *J Am Board Fam Pract*. 2001;14:211-218.
Inturrisi CE. Clinical pharmacology of opioids for pain. *Clin J Pain*. 2002;18(suppl 4):S3-S13.

McCarberg BH, Barkin RL. Long-acting opioids for chronic pain: pharmacotherapeutic opportunities to enhance compliance, quality of life, and analgesia. *Am J Ther*. 2001;8:181-186.
Thomsen AB, Becker N, Eriksen J. Opioid rotation in chronic non-malignant pain patients. A retrospective study. *Acta Anaesthesiol Scand*. 1999;43:918-923.



1. Katz N, Rauck R, Ahdieh H, et al. A 12-week, randomized, placebo-controlled trial assessing the safety and efficacy of oxymorphone extended release for opioid-naïve patients with chronic low back pain. *Curr Med Res Opin*. 2007;23:117-128.

OBJECTIVE: Determine the efficacy and tolerability of oxymorphone extended release (OPANA ER) in opioid-naive patients with moderate to severe chronic low back pain (CLBP). DESIGN AND METHODS: Patients > or = 18 years of age were titrated with oxymorphone ER (5- to 10-mg increments every 12 h, every 3-7 days) to a well-tolerated, stabilized dose. Patients were then randomized to continue their oxymorphone ER dose or receive placebo every 12 h for 12 weeks. Oxymorphone immediate release was available every 4-6 h, as needed, for the first 4 days and twice daily thereafter. RESULTS: Sixty-three percent of patients (205/325) were titrated to a stabilized dose of oxymorphone ER, most (203/205) within 1 month. During titration, 18% discontinued from adverse events (AEs) and 1% from lack of efficacy. For patients completing titration, average pain intensity decreased from 69.4 mm at screening to 22.7 mm ($p < 0.0001$). After randomization, 68% of oxymorphone ER and 47% of placebo patients completed 12 weeks of double-blind treatment. Approximately 8% of patients in each group discontinued because of AEs. Placebo patients discontinued significantly sooner from lack of efficacy than those receiving oxymorphone ER ($p < 0.0001$). Pain intensity increased significantly more in the placebo group (least squares [LS] mean change 26.9 +/- 2.4 [median 28.0]) than in the oxymorphone ER group (LS mean change 10.0 +/- 2.4 [median 2.0]; $p < 0.0001$). Oxymorphone ER was generally well tolerated without unexpected AEs. Although limitations of a randomized withdrawal study include the potential for unblinding and opioid withdrawal in placebo patients, opioid withdrawal was limited to two patients in the placebo group and one in the oxymorphone ER group. **CONCLUSIONS: Stabilized doses of oxymorphone ER were generally safe and effective over a 12-week double-blind treatment period in opioid-naive patients with CLBP.**

2. Perrot S, Krause D, Crozes P, Naïm C; GRTF-ZAL-1 Study Group. Efficacy and tolerability of paracetamol/tramadol (325 mg/37.5 mg) combination treatment compared with tramadol (50 mg) monotherapy in patients with subacute low back pain: a multicenter, randomized, double-blind, parallel-group, 10-day treatment study. Clin Ther. 2006 Oct;28(10):1592-1606.

OBJECTIVE: This study compared the efficacy and tolerability of PIT with tramadol alone (T) in patients with subacute LBP and assessed whether, under comparable analgesic conditions, PIT would be better tolerated. METHODS: This was a multicenter, randomized, double-blind, parallel-group study. Patients were enrolled if they suffered from nonspecific LBP lasting 10 to 42 days and experienced at least moderate pain (> or =40 mm on a 100-mm visual analog scale). Patients were randomized and treated for 10 days with PIT (325 mg/37.5 mg) or T (50 mg). The study outcomes were treatment efficacy (pain intensity, pain relief, patient satisfaction, physicians' assessment of pain control) and tolerability (adverse events [AEs], patients' tolerability judgment). RESULTS: A total of 119 patients were enrolled (PIT, n = 59; T, n = 60). Demographic characteristics of patients were comparable between the PIT and T groups in regard to age (mean, 56.5 vs 54.1 years, respectively), sex (women/men, 38121 vs 31129), race (white, 96.1% vs 94.2%), and body mass index (24.9 vs 26.1 kg/m2). Pain intensity (mean [SD] percentage of worst imaginable pain) improved from nearly identical levels at baseline (P/T, 67.5 [13.0] vs T, 65.3 [14.6]; P = NS) to similarly low levels at the final visit (P/T, 27.9 [22.7] vs T, 24.8 [21.6]; P = NS). The reduction in pain intensity was significant in both treatment groups (P < 0.001). Adequate pain relief (ie, "moderate," "important," or "complete") was observed in 81.6% (40149) of PIT patients versus 82.9% (39147) of T patients (P = NS). Comparably high rates of overall patient satisfaction (72.5% [37151] vs 72.9% [35148], respectively; P = NS) were achieved. Both treatment groups took a comparable number of daily units of study medication, which resulted in significantly (P < 0.001) lower daily doses of tramadol in the P/T group (mean [SD], 172.5 [46.6] mg) than in the T group (227.3 [59.7] mg). More P/T patients (84.3%) than T patients (68.8%) judged treatment tolerability as good or very good (P = NS). Significantly fewer AEs (P < 0.001) were observed in PIT patients, and the overall incidence of AEs (mostly opioid-typical AEs [eg, nausea, dizziness/vertigo, sleepiness/drowsiness, constipation, vomiting]) was much lower after P/T compared with T (P = 0.019). The most common AEs in the P/T and T groups were nausea (8159 vs 21160 patients, respectively; P = 0.012) and dizziness (3/59 vs 15/60 patients; P= 0.006). **CONCLUSIONS: Tramadol, alone and in combination with paracetamol, provided highly effective analgesia for these patients with subacute LSP.** However, the combination of PIT, which resulted in 25% less tramadol than equianalgesic daily doses of T alone, considerably reduced the incidence of AEs and improved tolerability.

3. Richards P, Zhang P, Friedman M, Dhanda R. Controlled-release oxycodone relieves moderate to severe pain in a 3-month study of persistent moderate to severe back pain [Abstract]. Pain Med. 2002;3:176.

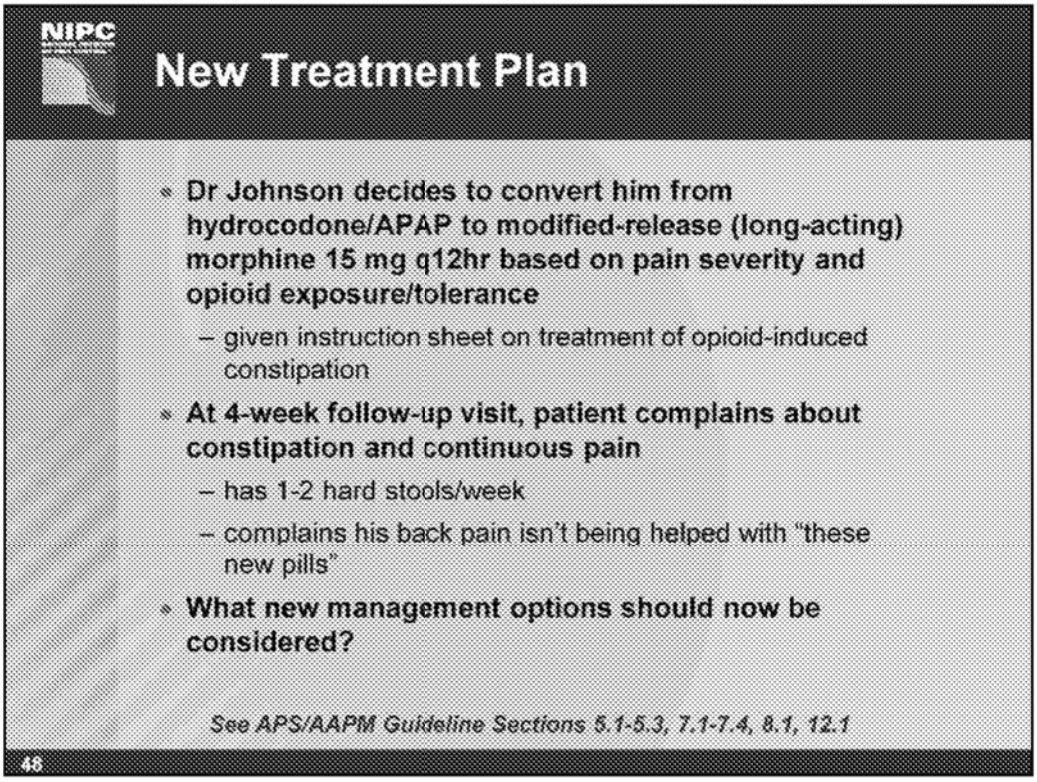
4. Allan L, Richarz U, Simpson K, Slappendel R. Transdermal fentanyl versus sustained release oral morphine in strong-opioid naïve patients with chronic low back pain. Spine. 2005;30:2484-2490.

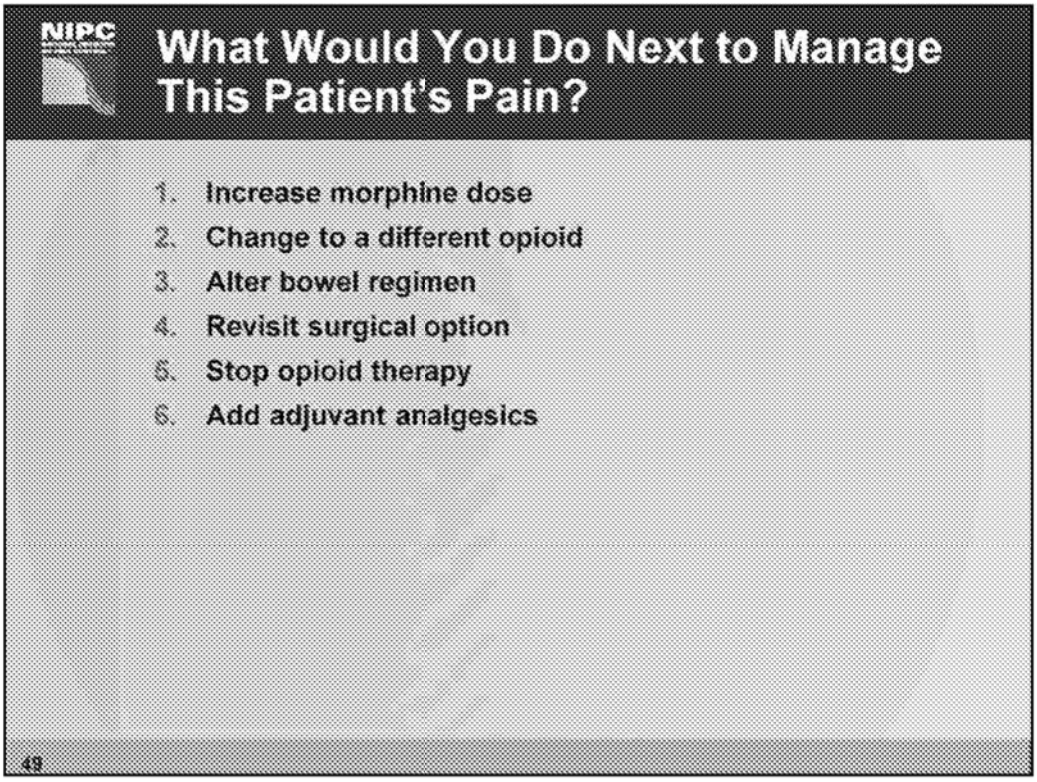
STUDY DESIGN: Open, randomized, parallel group multicenter study. OBJECTIVES: To compare the efficacy and safety of transdermal fentanyl (TDF) and sustained release morphine (SRM) in strong-opioid naïve patients with chronic low back pain (CLBP). SUMMARY OF BACKGROUND DATA: Most studies of TDF and SRM have involved patients already receiving strong opioids. This is the first large-scale study focusing on strong-opioid naïve patients with CLBP. METHODS: Adults with CLBP requiring regular strong opioid therapy received either TDF or SRM for 13 months. Starting doses were 25 microg/hr fentanyl patches every 72 hours or 30 mg oral morphine every 12 hours. Doses were adjusted according to response. Participants assessed pain relief and bowel function using weekly diaries. Other assessments, including quality of life, disease progression, and side effects, were made by patients and investigators. RESULTS: Data from 680 patients showed that TDF and SRM provided similar levels of pain relief, but TDF was associated with significantly less constipation than SRM, indicating a greater likelihood of satisfactory pain relief without unmanageable constipation for patients receiving TDF. Other ratings were similar for TDF and SRM, but TDF provided greater relief of pain at rest and at night. CONCLUSIONS: TDF and SRM provided equivalent levels of pain relief, but TDF was associated with less constipation. This study indicates that sustained-release strong opioids can safely be used in strong-opioid naïve patients.

5. Rauck RL, Bookbinder SA, Bunker TR, Alftine CD, Gershon S, de Jong E, Negro-Vilar A, Ghalie R. A randomized, open-label, multicenter trial comparing once-a-day AVINZA (morphine sulfate extended-release capsules) versus twice-a-day OxyContin (oxycodone hydrochloride controlled-release tablets) for the treatment of chronic, moderate to severe low back pain: improved physical functioning in the ACTION trial. *J Opioid Manag*. 2007;3:35-43.

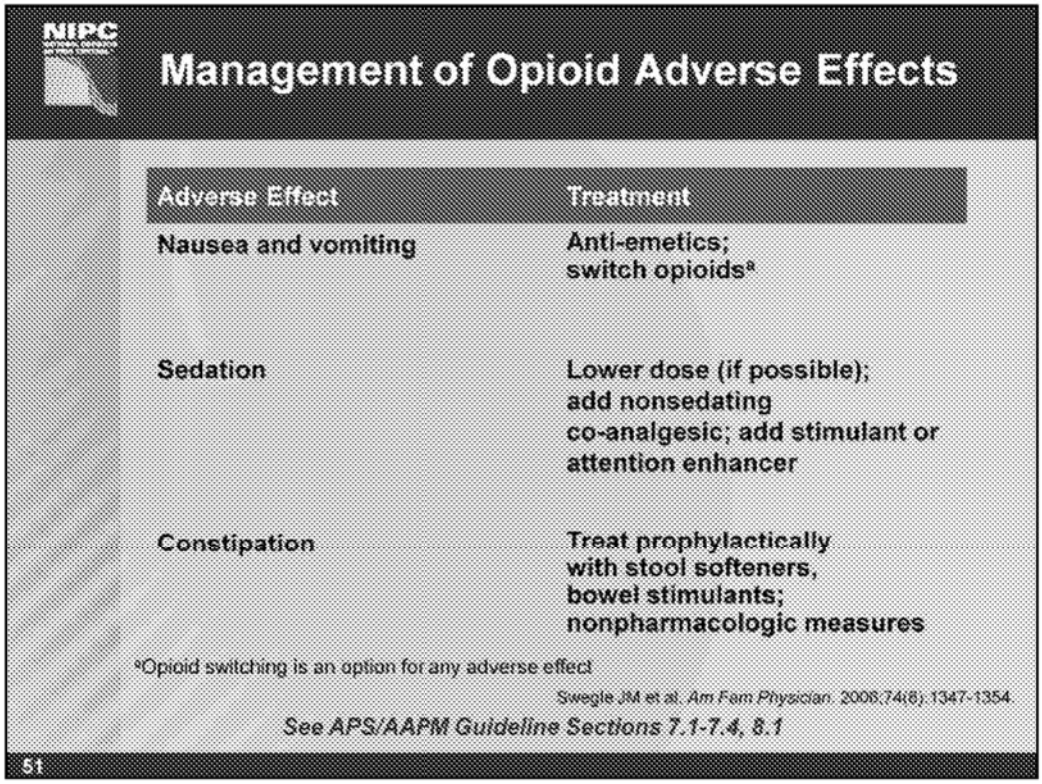
This multicenter trial compared the efficacy, safety, and effect on quality of life and work limitation of once-daily extended-release morphine sulfate capsules (AVINZA, A-MQD) and twice-daily controlled-release oxycodone HCl tablets (OxyContin, O-ER) in subjects with chronic, moderate to severe low back pain. After randomization and a period of opioid dose titration, subjects

(n=266) underwent an eight-week evaluation phase and an optional four-month extension phase (n=174 in extension phase). Subjects were assessed using the 12-item Short-Form Health Survey (SF-12) and the Work Limitations Questionnaire (WLQ). In both groups, significant improvements were observed in the SF-12 mean scores for physical functioning ($p < 0.001$), role physical ($p < 0.0001$), bodily pain ($p < 0.0001$), physical summary ($p < 0.001$), and mental component summary ($p < 0.005$). At the end of the titration period, greater relative improvements from baseline were seen in the SF-12 section on physical components in the A-MQD group versus the O-ER group, with significant differences observed for physical functioning ($p = 0.0374$), role physical ($p = 0.0341$), bodily pain ($p = 0.0001$), and physical summary ($p = 0.0022$). In both groups, SF-12 mean scores improved significantly for mental health ($p < 0.01$), role emotional ($p < 0.01$), social functioning ($p < 0.0005$), vitality ($p < 0.005$), and the mental component summary ($p < 0.005$), but no significant differences were noted between the two groups. Both groups reported improvement from baseline in WLQ physical demands scores, with no significant differences noted between the two groups. At the end of the evaluation phase, fewer subjects were unable to work due to illness or treatment in the A-MQD group than in the O-ER group (8.5 percent versus 19.4 percent, respectively; $p = 0.0149$). In conclusion, **compared to twice-daily OxyContin, once-daily AVINZA resulted in significantly better and earlier improvement of physical function and ability to work.**


NIPC
New Treatment Plan
Dr Johnson decides to convert him from hydrocodone/APAP to modified-release (long-acting) morphine 15 mg q12hr based on pain severity and opioid exposure/tolerance
– given instruction sheet on treatment of opioid-induced constipation
At 4-week follow-up visit, patient complains about constipation and continuous pain
– has 1-2 hard stools/week
– complains his back pain isn't being helped with "these new pills"
What new management options should now be considered?
See APS/AAPM Guideline Sections 5.1-5.3, 7.1-7.4, 8.1, 12.1
48


NIPC
What Would You Do Next to Manage This Patient's Pain?
1. Increase morphine dose
2. Change to a different opioid
3. Alter bowel regimen
4. Revisit surgical option
5. Stop opioid therapy
6. Add adjuvant analgesics
49


NIPC
Multiple Options Are Appropriate for Managing Patient's Current Problems
1. Increasing dose of morphine may improve pain control
2. Rotation of opioid may be indicated if compliance is a problem due to adverse-effect burden
3. Since constipation is a chronic problem related to opioid therapy, aggressive and early management is important for compliance
4. Surgical consideration is not an option for this patient
5. Stopping opioid therapy is premature
6. Addition of an adjuvant agent may be indicated after reassessment of patient to determine whether current pain is responsive to therapy
50



Side effects may include nausea, vomiting, itching, sedation, balance/ataxia (especially in older patients) and pruritus. Cognitive impairments/mental "clouding" may also occur. However, tolerance to these side effects typically occurs within a few days to weeks of therapy initiation. The most common side effect of chronic opioid therapy is constipation, which may persist, particularly if there are other predisposing causes.

Once ruling out other causes, opioid side effects may be ameliorated by a number of approaches. For nausea, first try switching opioids and then try anti-emetics. For nausea associated with vertigo or movement, try antivertiginous agents (eg, scopolamine); for nausea associated with satiety, try metoclopramide.

For sedation/somnolence, lower dose if possible; or add co-analgesics or psychostimulant agents. Modifications in the patient's diet and activity levels may also be beneficial.

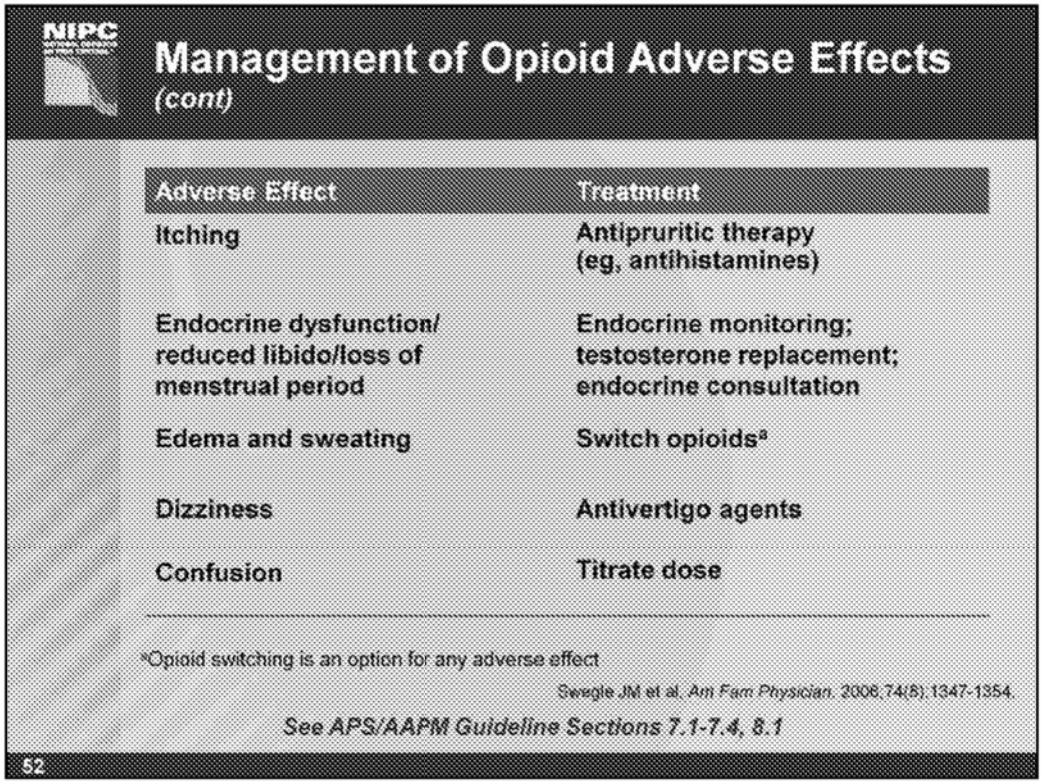
For constipation, treat prophylactically with stool softeners, intermittent stimulant laxatives such as docusate (at least 250 mg/d) or other osmotic laxatives and senna, and nonpharmacologic measures, or try switching opioids. Patient should be counseled to optimize fluids and fiber in diet.

Portenoy RK. Opioid analgesics. In: Portenoy RK, Kanner RM, eds. *Pain Management: Theory and Practice*. Philadelphia, Pa: F.A. Davis Company;1996:248-253.

Opioid analgesics are useful agents for treating pain of various etiologies; however, adverse effects are potential limitations to their use. Strategies to minimize adverse effects of opioids include dose reduction, symptomatic management, opioid rotation, and changing the route of administration. Nausea occurs in approximately 25 percent of patients; prophylactic measures may not be required. Patients who do develop nausea will require antiemetic treatment with an antipsychotic, prokinetic agent, or serotonin antagonist. Understanding the mechanism for opioid-induced nausea will aid in the selection of appropriate agents. Constipation is considered an expected side effect with chronic opioid use. Physicians should minimize the development of constipation using prophylactic measures. Monotherapy with stool softeners often is not effective; a stool softener combined with a stimulant laxative is preferred. Sedation and cognitive changes occur with initiation of therapy or dose escalation. Underlying disease states or other centrally acting medications often will compound the opioid's adverse effects. Minimizing unnecessary medications and judicious use of stimulants and antipsychotics are used to manage the central nervous system side effects. Pruritus may develop, but it is generally not considered an allergic reaction. Antihistamines are the preferred

management option should pharmacotherapy treatment be required.

Swegle JM, Logemann C. Management of common opioid-induced adverse effects. Am Fam Physician. 2006 Oct 15;74(8):1347-1354.



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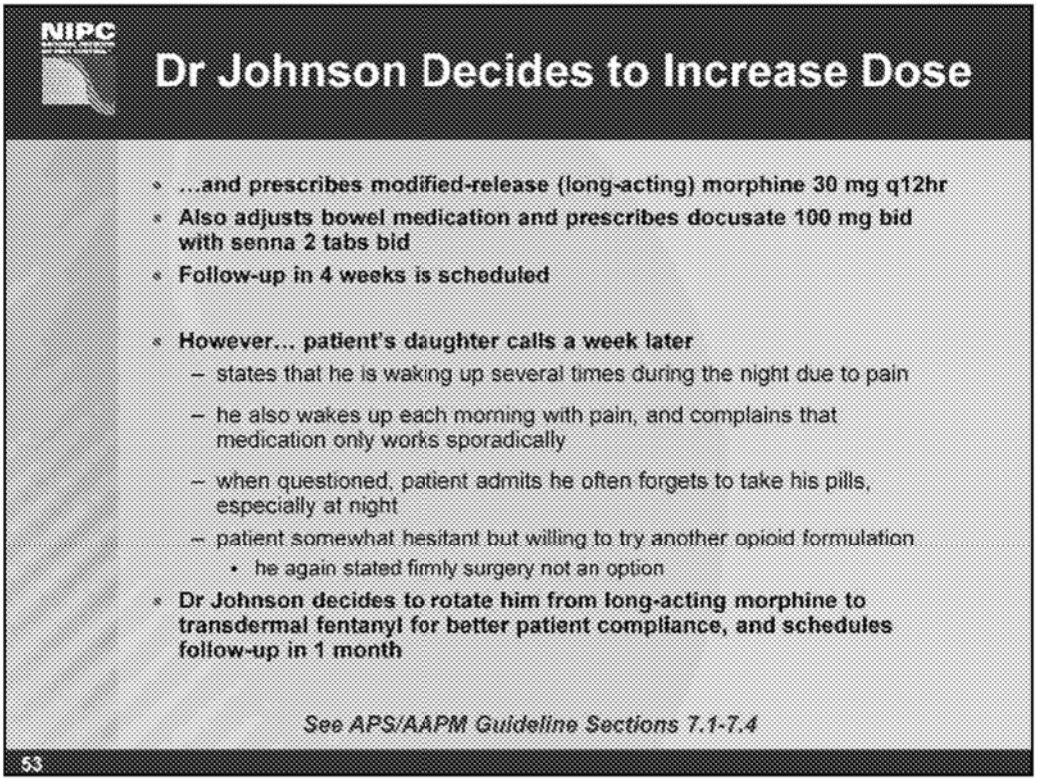
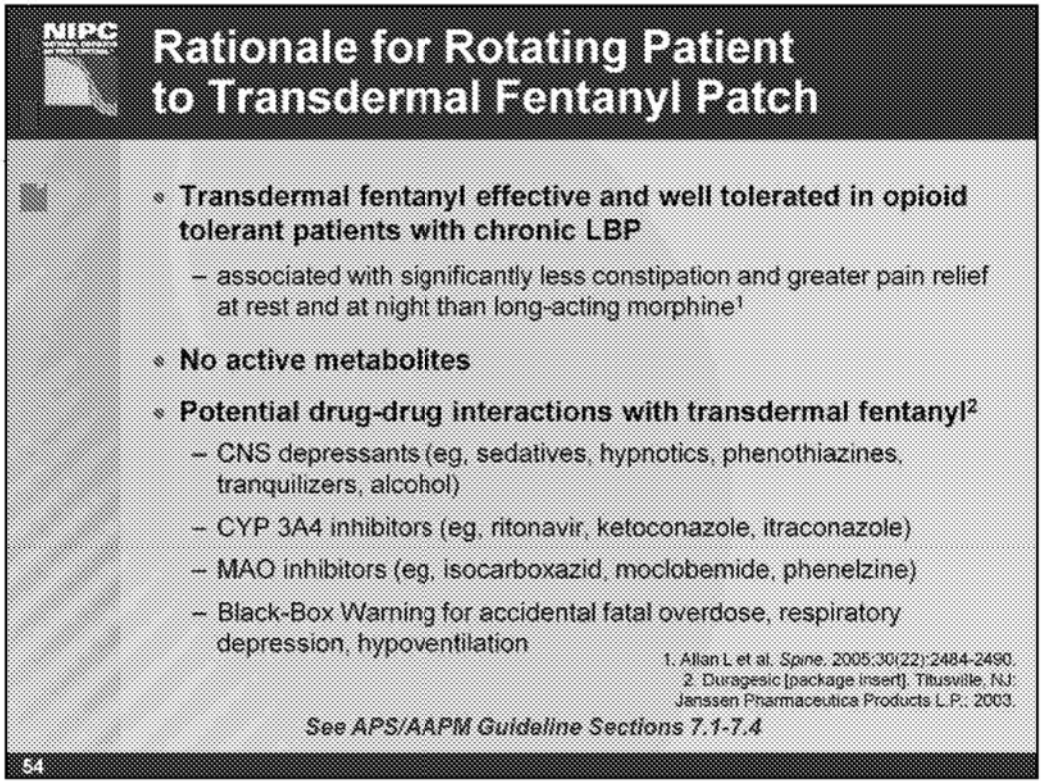

NIPC
Dr Johnson Decides to Increase Dose
...and prescribes modified-release (long-acting) morphine 30 mg q12hr
Also adjusts bowel medication and prescribes docusate 100 mg bid with senna 2 tabs bid
Follow-up in 4 weeks is scheduled
However... patient's daughter calls a week later
states that he is waking up several times during the night due to pain
he also wakes up each morning with pain, and complains that medication only works sporadically
when questioned, patient admits he often forgets to take his pills, especially at night
patient somewhat hesitant but willing to try another opioid formulation
he again stated firmly surgery not an option
Dr Johnson decides to rotate him from long-acting morphine to transdermal fentanyl for better patient compliance, and schedules follow-up in 1 month
See APS/AAPM Guideline Sections 7.1-7.4
53



1. Allan L, Richarz U, Simpson K, Slappendel R. Transdermal fentanyl versus sustained release oral morphine in strong-opioid naïve patients with chronic low back pain. *Spine*. 2005;30:2484-2490.

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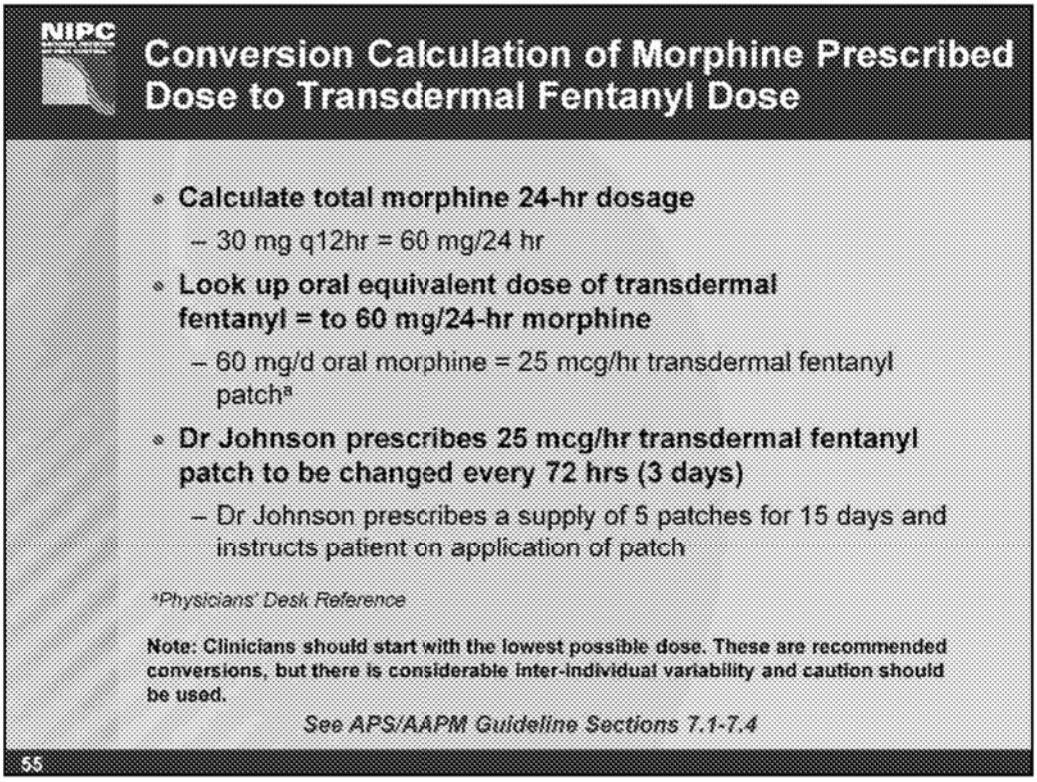
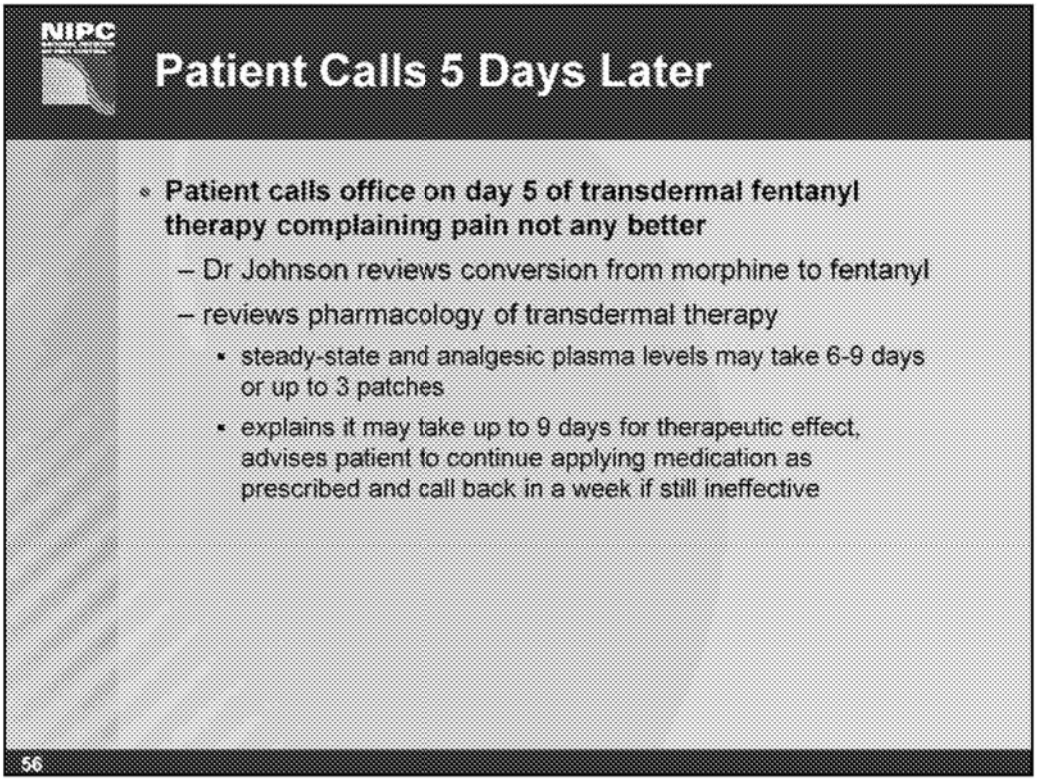
2. Duragesic Prescribing Information. Available at: http://www.fda.gov/cder/foi/label/2005/19813s039lbl.pdf. Accessed June 22, 2007.


NIPC
Conversion Calculation of Morphine Prescribed Dose to Transdermal Fentanyl Dose
Calculate total morphine 24-hr dosage
– 30 mg q12hr = 60 mg/24 hr
Look up oral equivalent dose of transdermal fentanyl = to 60 mg/24-hr morphine
– 60 mg/d oral morphine = 25 mcg/hr transdermal fentanyl patch[a]
Dr Johnson prescribes 25 mcg/hr transdermal fentanyl patch to be changed every 72 hrs (3 days)
– Dr Johnson prescribes a supply of 5 patches for 15 days and instructs patient on application of patch
[a]Physicians' Desk Reference
Note: Clinicians should start with the lowest possible dose. These are recommended conversions, but there is considerable inter-individual variability and caution should be used.
See APS/AAPM Guideline Sections 7.1-7.4
55


NIPC
Patient Calls 5 Days Later
Patient calls office on day 5 of transdermal fentanyl therapy complaining pain not any better
– Dr Johnson reviews conversion from morphine to fentanyl
– reviews pharmacology of transdermal therapy
• steady-state and analgesic plasma levels may take 6-9 days or up to 3 patches
• explains it may take up to 9 days for therapeutic effect, advises patient to continue applying medication as prescribed and call back in a week if still ineffective
56

NIPC

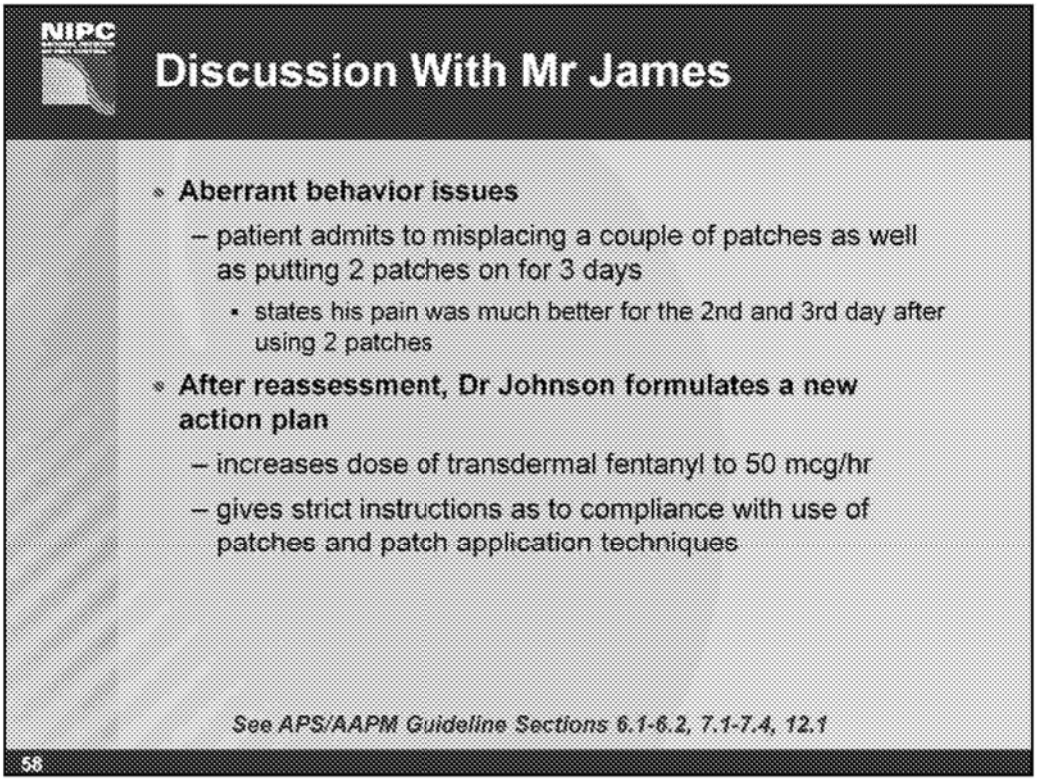
Follow-up Visit 1 Month Later

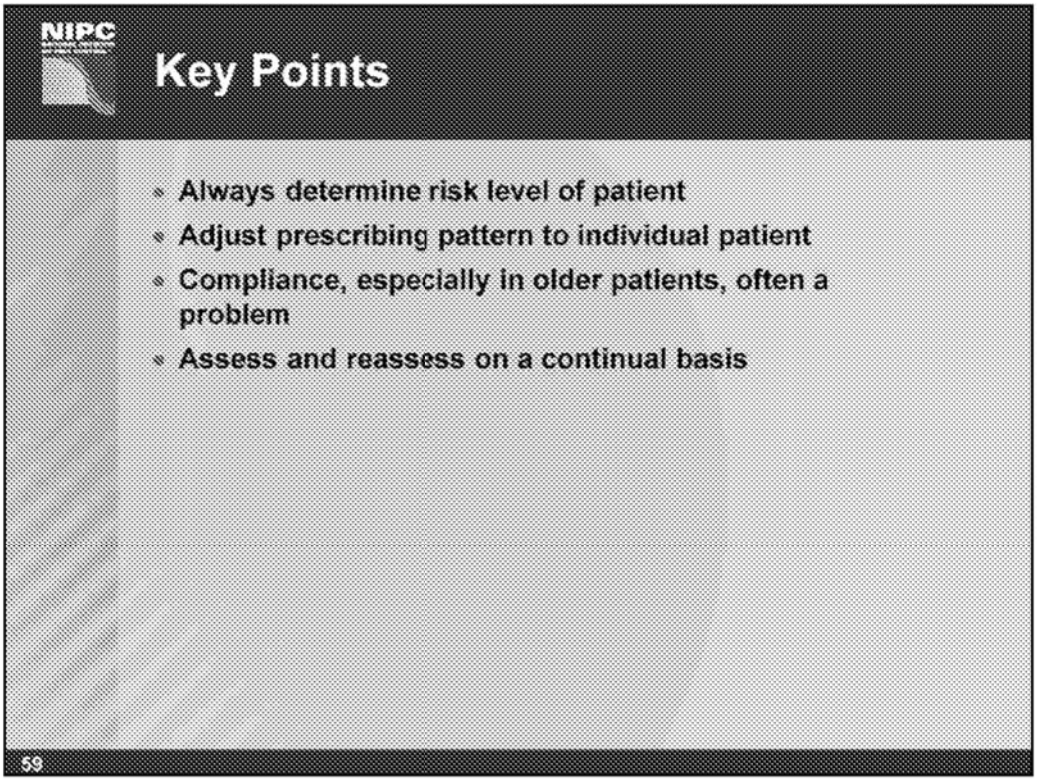
"A's" Reassessment Chart Note

- Analgesia: Average nighttime pain 4/10; daytime activity-related pain 6/10
- AEs: Constipation improved, 3-4 bowel movements per week; slight redness at patch application site
- ADLs: Still not happy due to inability to work in garden; sleep has improved, only waking 1x per night
- Aberrant Drug-Taking Behavior: Complains that patches sometimes fell off after 1 day and he ran out of patches 6 days early
- Assessment Impression: Good nighttime pain control; still problem with pain during the day
- Action Plan: Discuss patch application technique with patient and problem with running out of patches early

See APS/AAPM Guideline Sections 5.1-5.3, 7.1-7.4

57


NIPC
Discussion With Mr James
Aberrant behavior issues
– patient admits to misplacing a couple of patches as well as putting 2 patches on for 3 days
▪ states his pain was much better for the 2nd and 3rd day after using 2 patches
After reassessment, Dr Johnson formulates a new action plan
– increases dose of transdermal fentanyl to 50 mcg/hr
– gives strict instructions as to compliance with use of patches and patch application techniques
See APS/AAPM Guideline Sections 6.1-6.2, 7.1-7.4, 12.1
58

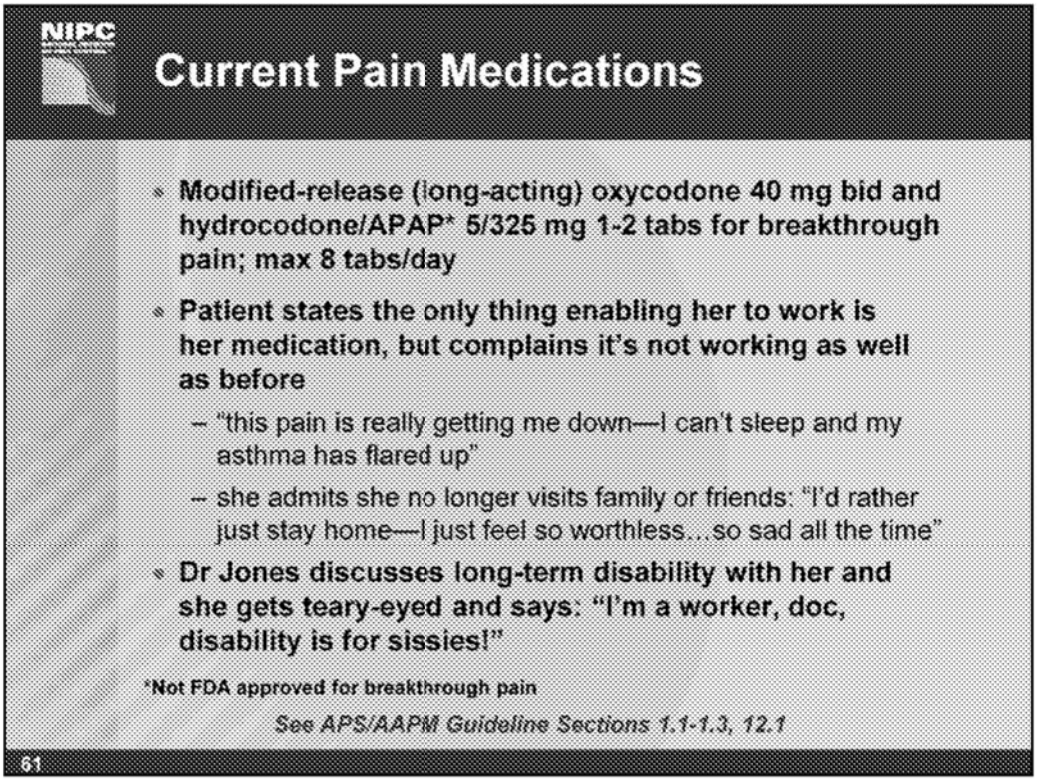

NIPC
Key Points
Always determine risk level of patient
Adjust prescribing pattern to individual patient
Compliance, especially in older patients, often a problem
Assess and reassess on a continual basis
59

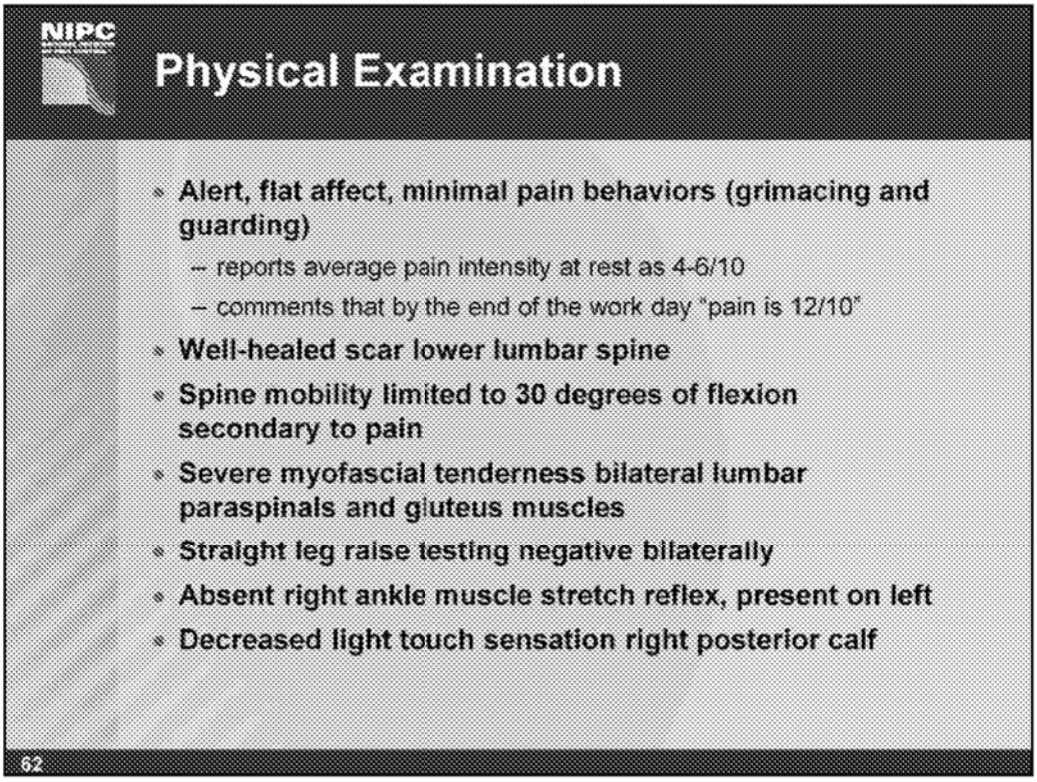
NIPC

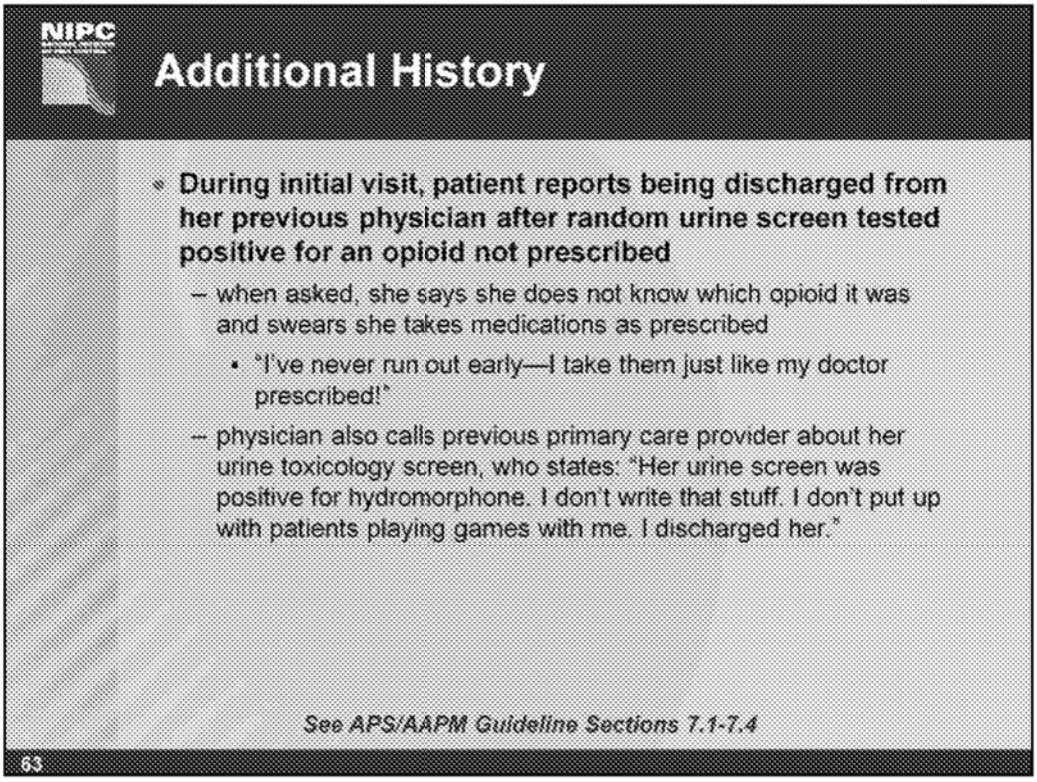
Meet Carla, Dr Jones's Patient

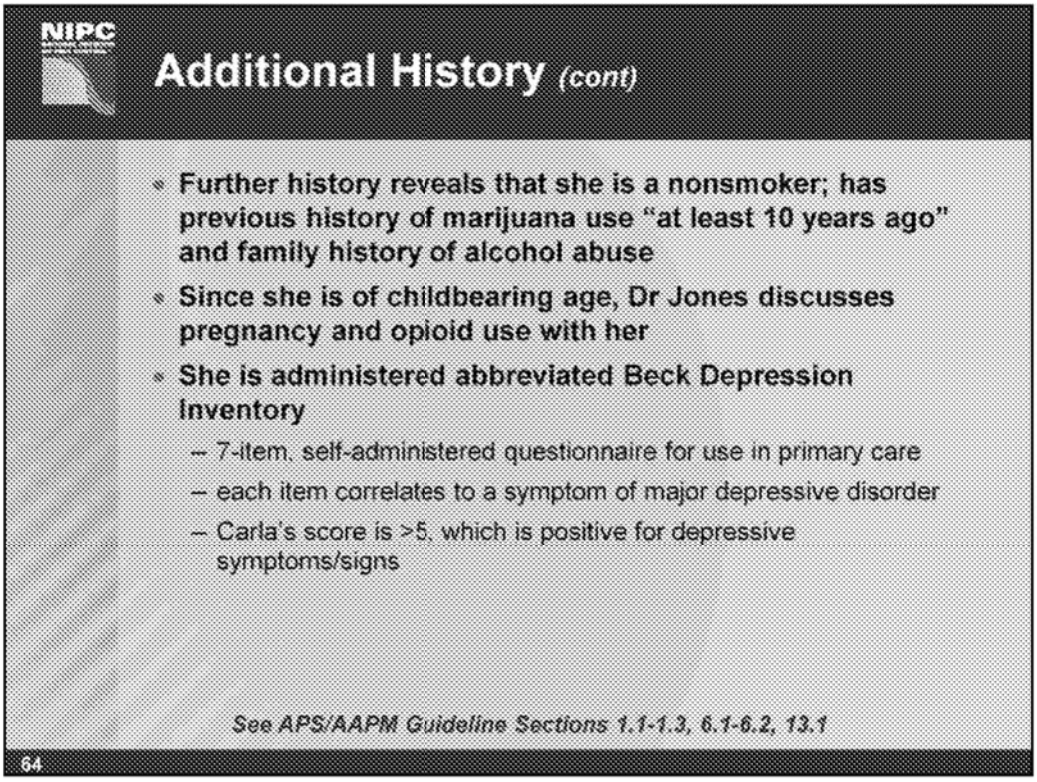
- 44-year-old female with debilitating LBP
- Initial surgery unsuccessful, as were other treatment attempts with NSAIDs, muscle relaxants, interventional spine procedures, and acupuncture
- Underwent second back surgery 4 yrs ago
  - fusion performed but only partially successful
  - she now complains of persistent right posterior thigh and calf pain
  - continuing pain interferes more and more with work delivering mail for post office

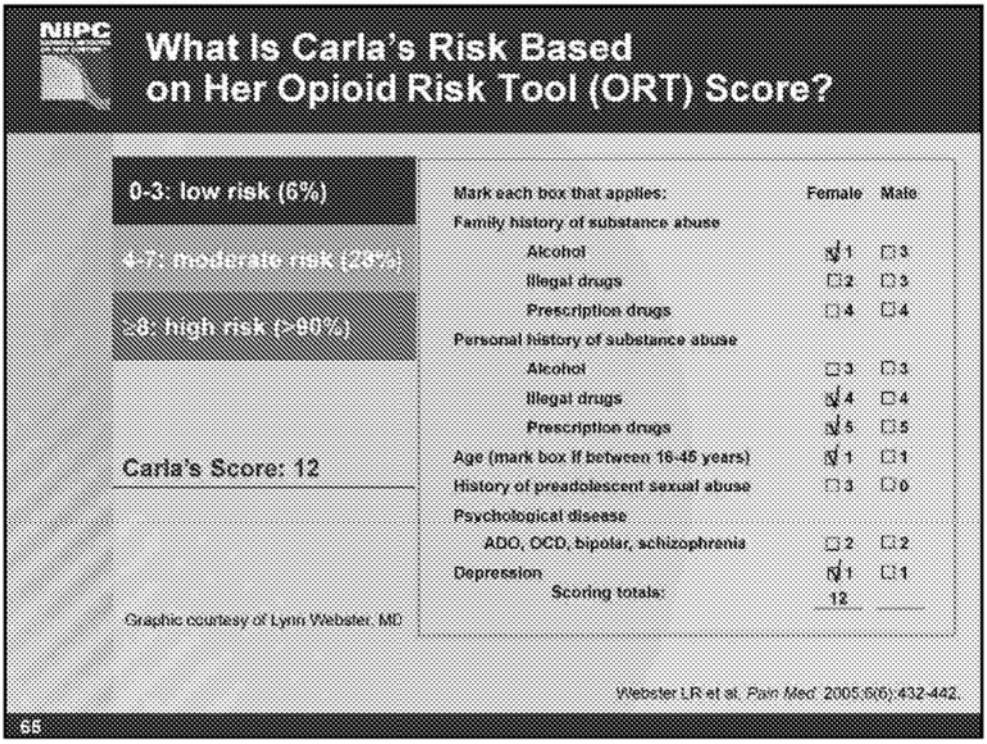
60


NIPC
Current Pain Medications
Modified-release (long-acting) oxycodone 40 mg bid and hydrocodone/APAP* 5/325 mg 1-2 tabs for breakthrough pain; max 8 tabs/day
Patient states the only thing enabling her to work is her medication, but complains it's not working as well as before
– "this pain is really getting me down—I can't sleep and my asthma has flared up"
– she admits she no longer visits family or friends: "I'd rather just stay home—I just feel so worthless…so sad all the time"
Dr Jones discusses long-term disability with her and she gets teary-eyed and says: "I'm a worker, doc, disability is for sissies!"
*Not FDA approved for breakthrough pain
See APS/AAPM Guideline Sections 1.1-1.3, 12.1
61

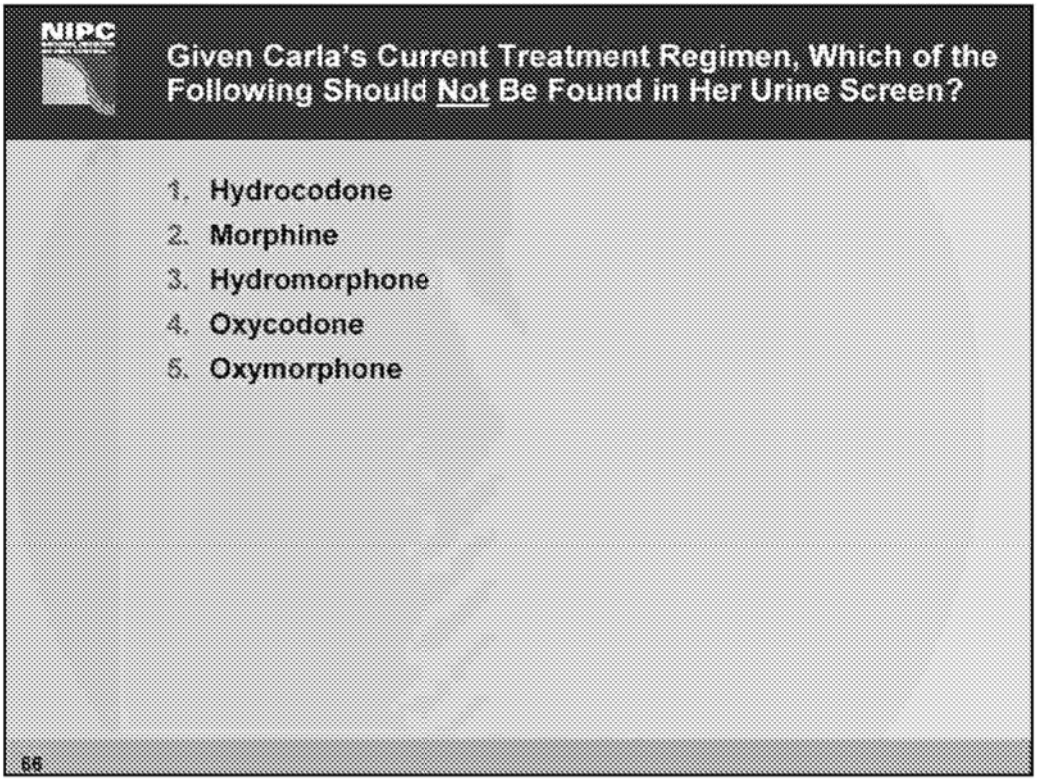

NIPC
Physical Examination
Alert, flat affect, minimal pain behaviors (grimacing and guarding)
– reports average pain intensity at rest as 4-6/10
– comments that by the end of the work day "pain is 12/10"
Well-healed scar lower lumbar spine
Spine mobility limited to 30 degrees of flexion secondary to pain
Severe myofascial tenderness bilateral lumbar paraspinals and gluteus muscles
Straight leg raise testing negative bilaterally
Absent right ankle muscle stretch reflex, present on left
Decreased light touch sensation right posterior calf
62

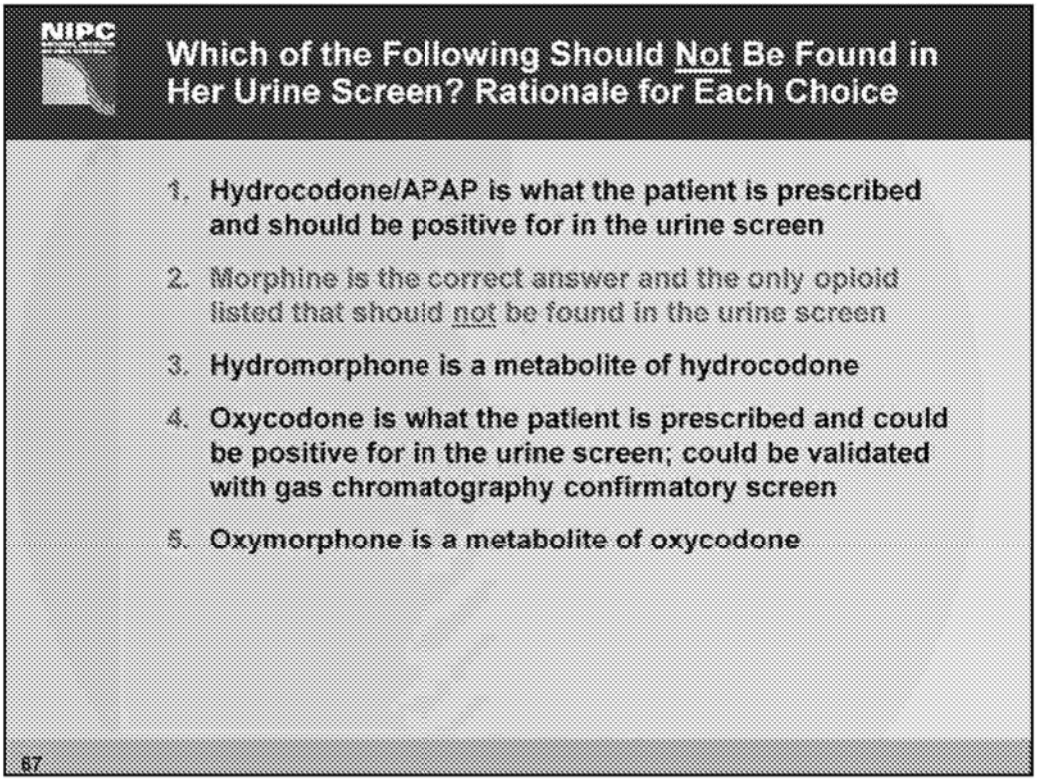

NIPC
Additional History
During initial visit, patient reports being discharged from her previous physician after random urine screen tested positive for an opioid not prescribed
– when asked, she says she does not know which opioid it was and swears she takes medications as prescribed
• "I've never run out early—I take them just like my doctor prescribed!"
– physician also calls previous primary care provider about her urine toxicology screen, who states: "Her urine screen was positive for hydromorphone. I don't write that stuff. I don't put up with patients playing games with me. I discharged her."
See APS/AAPM Guideline Sections 7.1-7.4
63

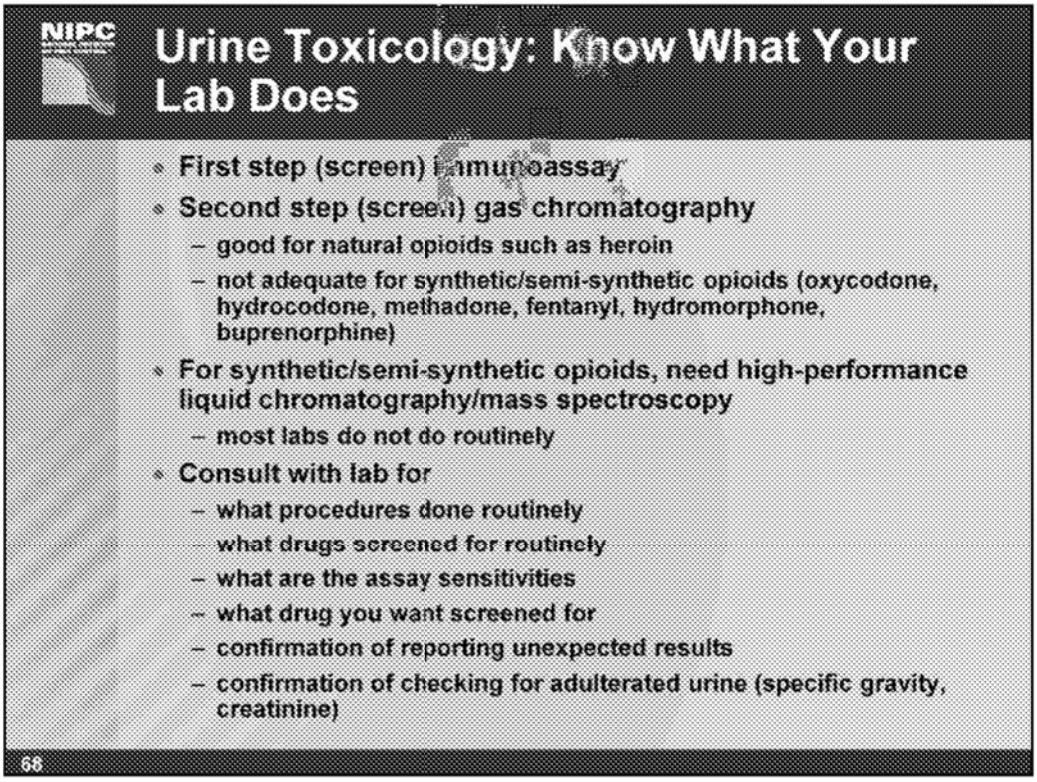

NIPC
Additional History (cont)
Further history reveals that she is a nonsmoker; has previous history of marijuana use "at least 10 years ago" and family history of alcohol abuse
Since she is of childbearing age, Dr Jones discusses pregnancy and opioid use with her
She is administered abbreviated Beck Depression Inventory
– 7-item, self-administered questionnaire for use in primary care
– each item correlates to a symptom of major depressive disorder
– Carla's score is >5, which is positive for depressive symptoms/signs
See APS/AAPM Guideline Sections 1.1-1.3, 6.1-6.2, 13.1
64

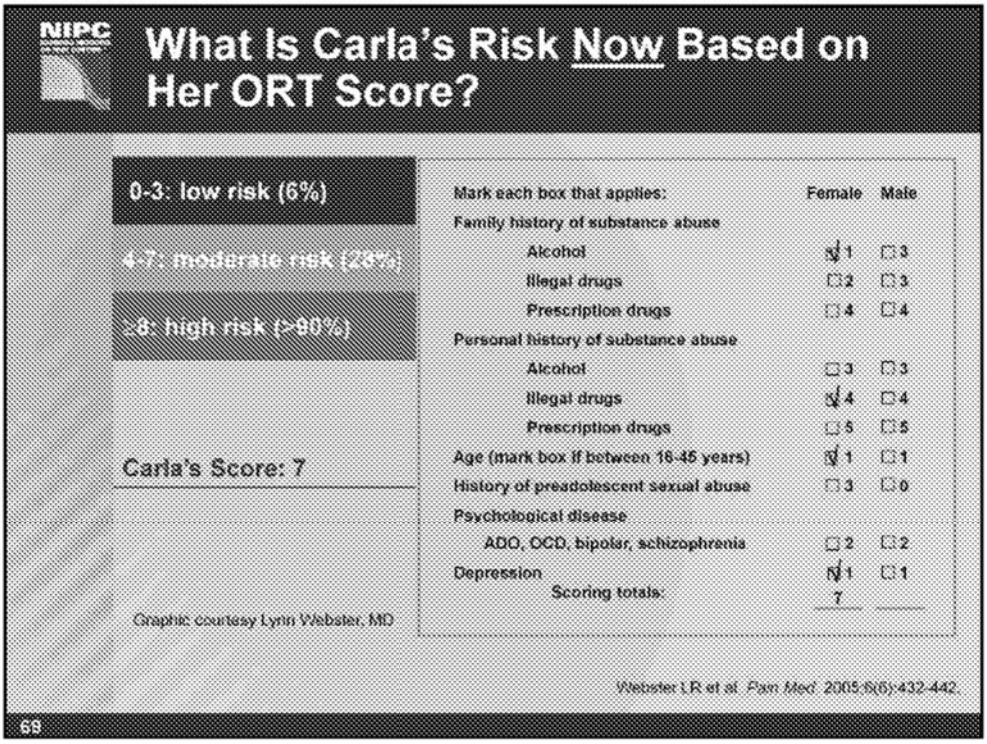


Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med*. 2005;6(6):432-442.

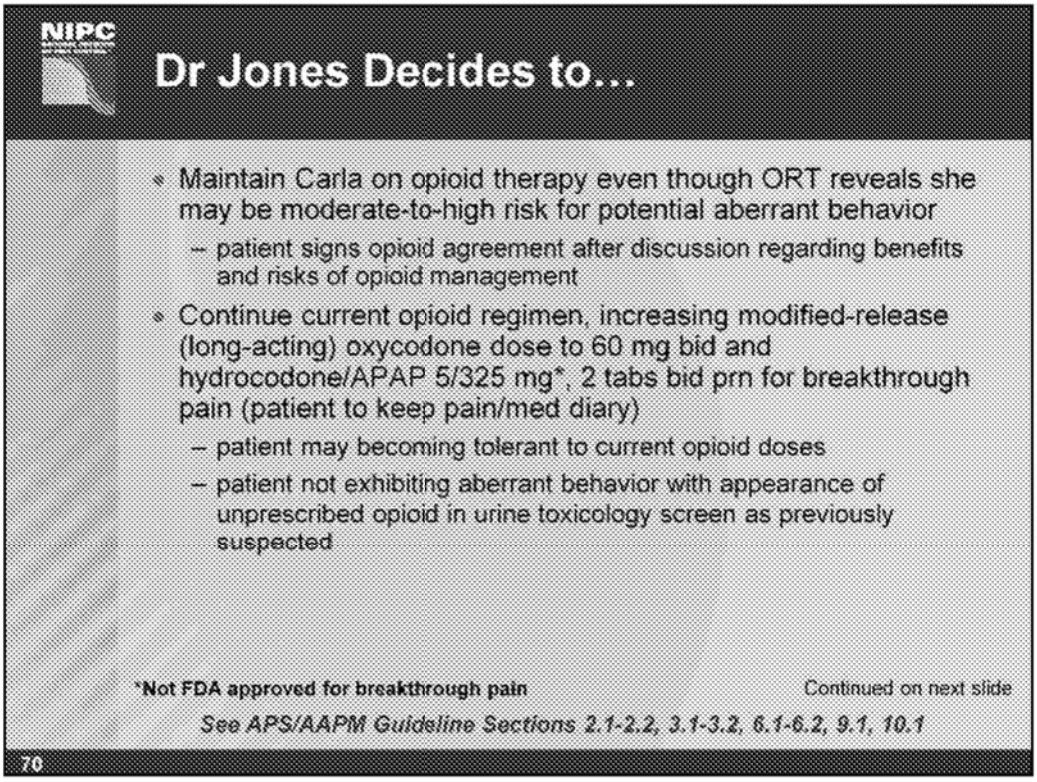

NIPC
Given Carla's Current Treatment Regimen, Which of the Following Should Not Be Found in Her Urine Screen?
1. Hydrocodone
2. Morphine
3. Hydromorphone
4. Oxycodone
5. Oxymorphone
66

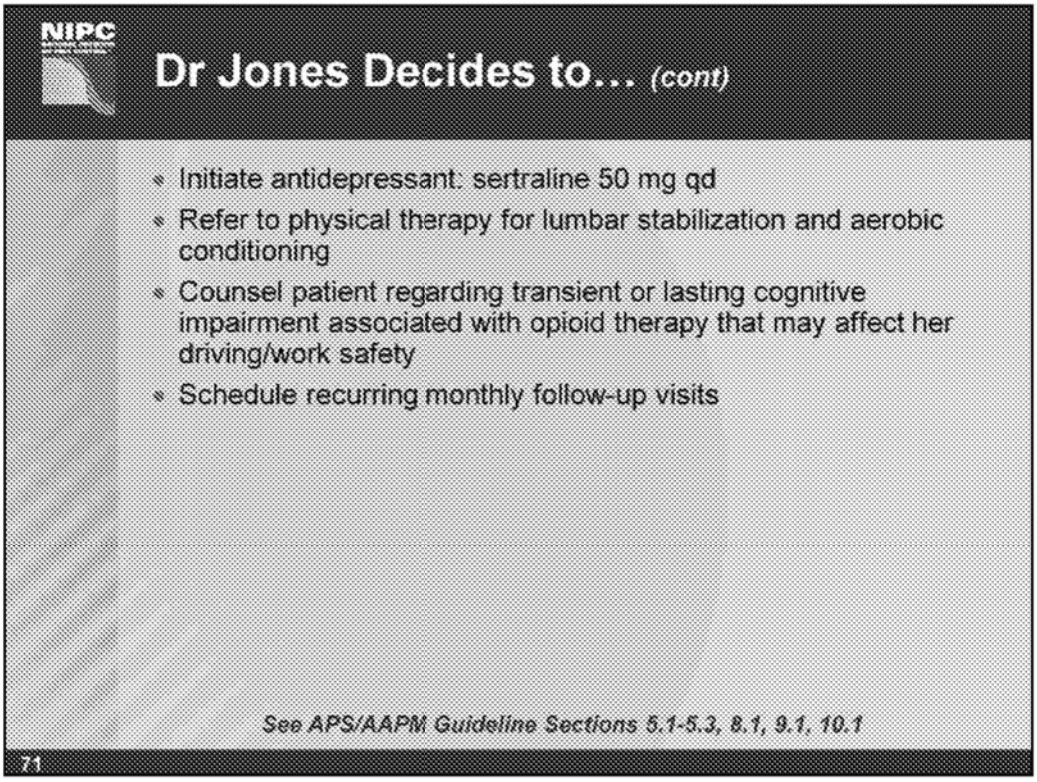

NIPC
Which of the Following Should Not Be Found in Her Urine Screen? Rationale for Each Choice
1. Hydrocodone/APAP is what the patient is prescribed and should be positive for in the urine screen
2. Morphine is the correct answer and the only opioid listed that should not be found in the urine screen
3. Hydromorphone is a metabolite of hydrocodone
4. Oxycodone is what the patient is prescribed and could be positive for in the urine screen; could be validated with gas chromatography confirmatory screen
5. Oxymorphone is a metabolite of oxycodone
67

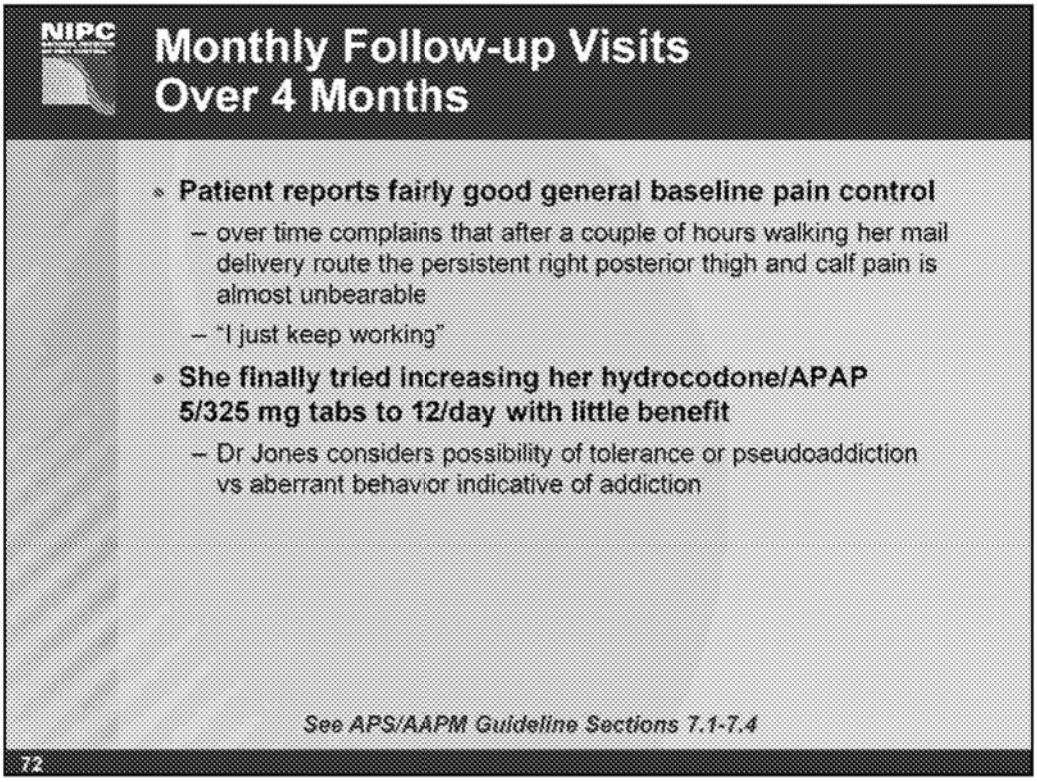

NIPC
Urine Toxicology: Know What Your Lab Does
First step (screen) immunoassay
Second step (screen) gas chromatography
good for natural opioids such as heroin
not adequate for synthetic/semi-synthetic opioids (oxycodone, hydrocodone, methadone, fentanyl, hydromorphone, buprenorphine)
For synthetic/semi-synthetic opioids, need high-performance liquid chromatography/mass spectroscopy
most labs do not do routinely
Consult with lab for
what procedures done routinely
what drugs screened for routinely
what are the assay sensitivities
what drug you want screened for
confirmation of reporting unexpected results
confirmation of checking for adulterated urine (specific gravity, creatinine)
68

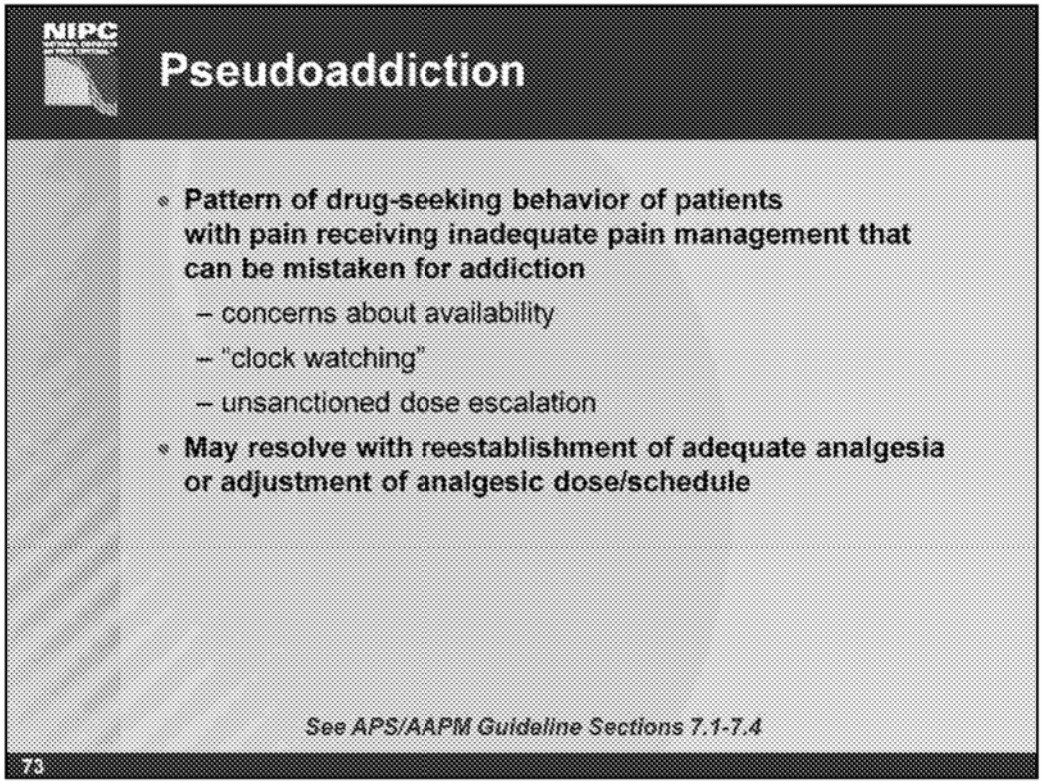


Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med*. 2005;6(6):432-442.


NIPC
Dr Jones Decides to…
Maintain Carla on opioid therapy even though ORT reveals she may be moderate-to-high risk for potential aberrant behavior
– patient signs opioid agreement after discussion regarding benefits and risks of opioid management
Continue current opioid regimen, increasing modified-release (long-acting) oxycodone dose to 60 mg bid and hydrocodone/APAP 5/325 mg*, 2 tabs bid prn for breakthrough pain (patient to keep pain/med diary)
– patient may becoming tolerant to current opioid doses
– patient not exhibiting aberrant behavior with appearance of unprescribed opioid in urine toxicology screen as previously suspected
*Not FDA approved for breakthrough pain
Continued on next slide
See APS/AAPM Guideline Sections 2.1-2.2, 3.1-3.2, 6.1-6.2, 9.1, 10.1
70


NIPC
Dr Jones Decides to… (cont)
Initiate antidepressant: sertraline 50 mg qd
Refer to physical therapy for lumbar stabilization and aerobic conditioning
Counsel patient regarding transient or lasting cognitive impairment associated with opioid therapy that may affect her driving/work safety
Schedule recurring monthly follow-up visits
See APS/AAPM Guideline Sections 5.1-5.3, 8.1, 9.1, 10.1
71


NIPC
Monthly Follow-up Visits
Over 4 Months
Patient reports fairly good general baseline pain control
over time complains that after a couple of hours walking her mail delivery route the persistent right posterior thigh and calf pain is almost unbearable
"I just keep working"
She finally tried increasing her hydrocodone/APAP 5/325 mg tabs to 12/day with little benefit
Dr Jones considers possibility of tolerance or pseudoaddiction vs aberrant behavior indicative of addiction
See APS/AAPM Guideline Sections 7.1-7.4
72



For patients with continuous pain, inadequate pain management (eg, prn dosing schedule, use of drugs with inadequate potency, use of dosing intervals that are too long) can lead to behavioral symptoms that mimic those seen with psychological dependence and can be mistaken for addiction.

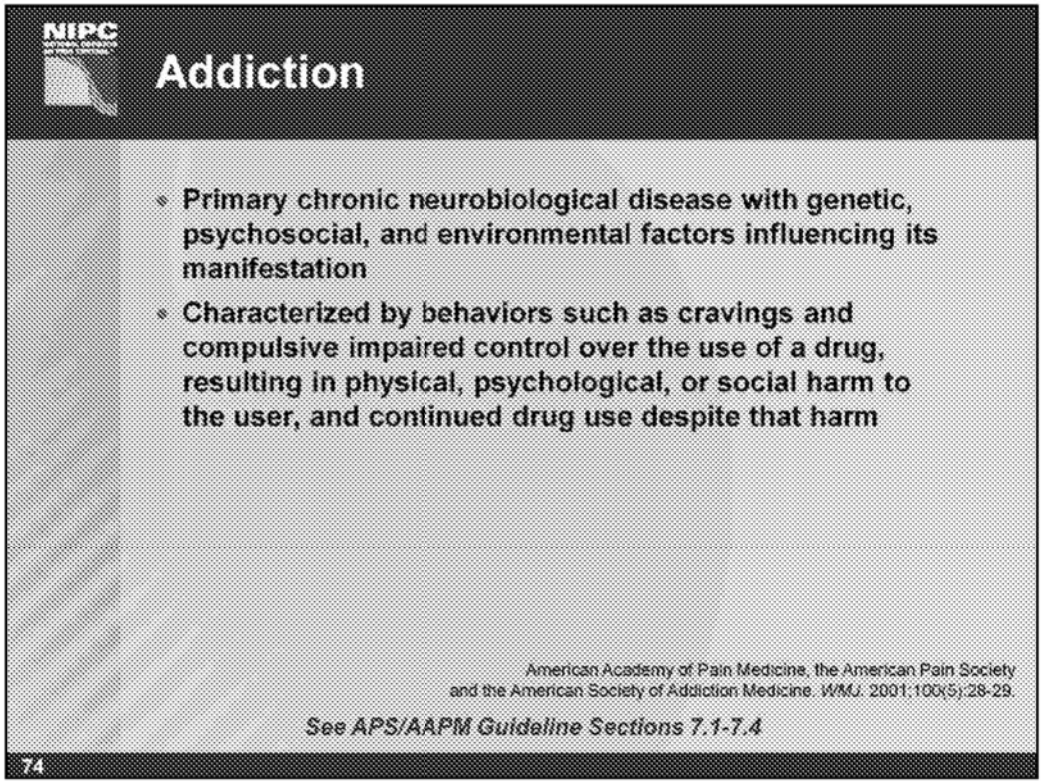
These may include cravings and aberrant behavior, concerns about drug availability, clock watching, and unsanctioned dose escalation.

In the case of pseudoaddiction, the problem behaviors resolve after sufficient pain relief is established.

However, behaviors related to true addiction may also resolve after dose escalation.

Thus, it can be difficult to distinguish pseudoaddiction from true addiction, and may require careful evaluation and management until the circumstances are sorted out. For example, it may be helpful to raise the dose and switch to a long-acting opioid but only give the patient a week's prescription at a time.

Weissman DE, Haddox JD. Opioid pseudoaddiction—an iatrogenic syndrome. *Pain*. 1989;36:363-366.



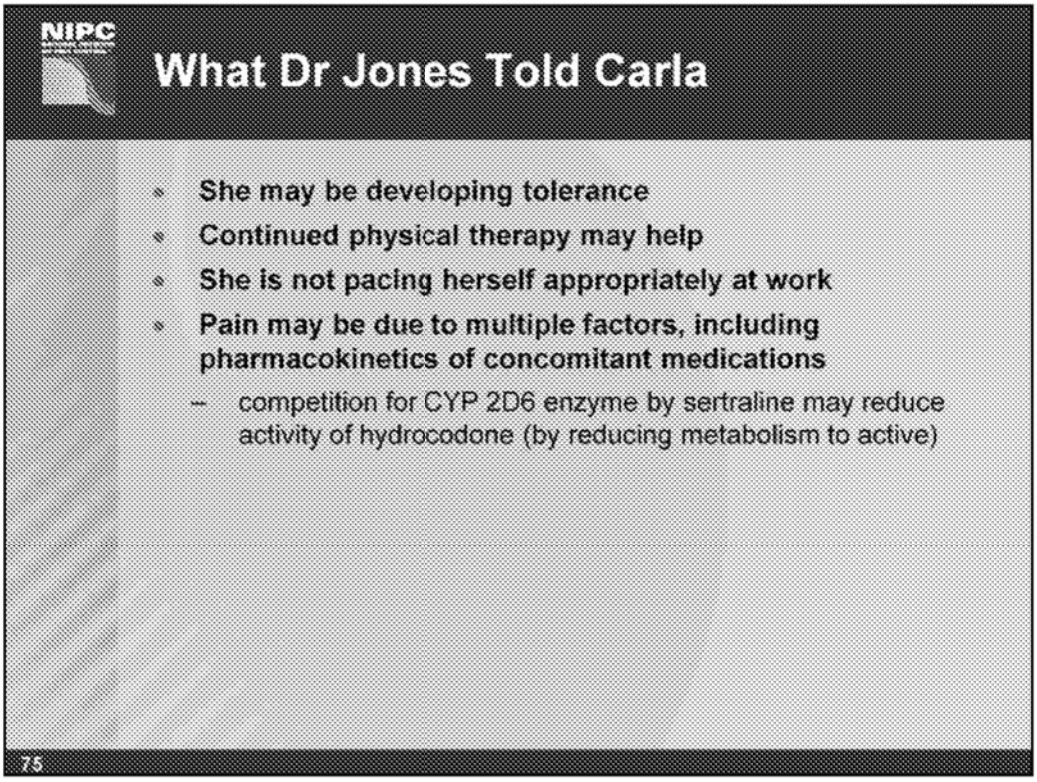
The identification of the disease of addiction is important to safe and effective clinical management of pain in individuals with addictive disorders. The disease of addiction affects approximately 10% of the general population, and its prevalence may be higher in subpopulations of patients with pain. The presence of active addiction may facilitate the experience of pain. Both active and recovering addiction may complicate the use of medications, such as opioids, important to the management of pain. There is, further, persistent misunderstanding among healthcare providers, regulators, and the general population regarding the nature and manifestations of addiction that may result in undertreatment of pain and stigmatization of patients using opioids for pain control.

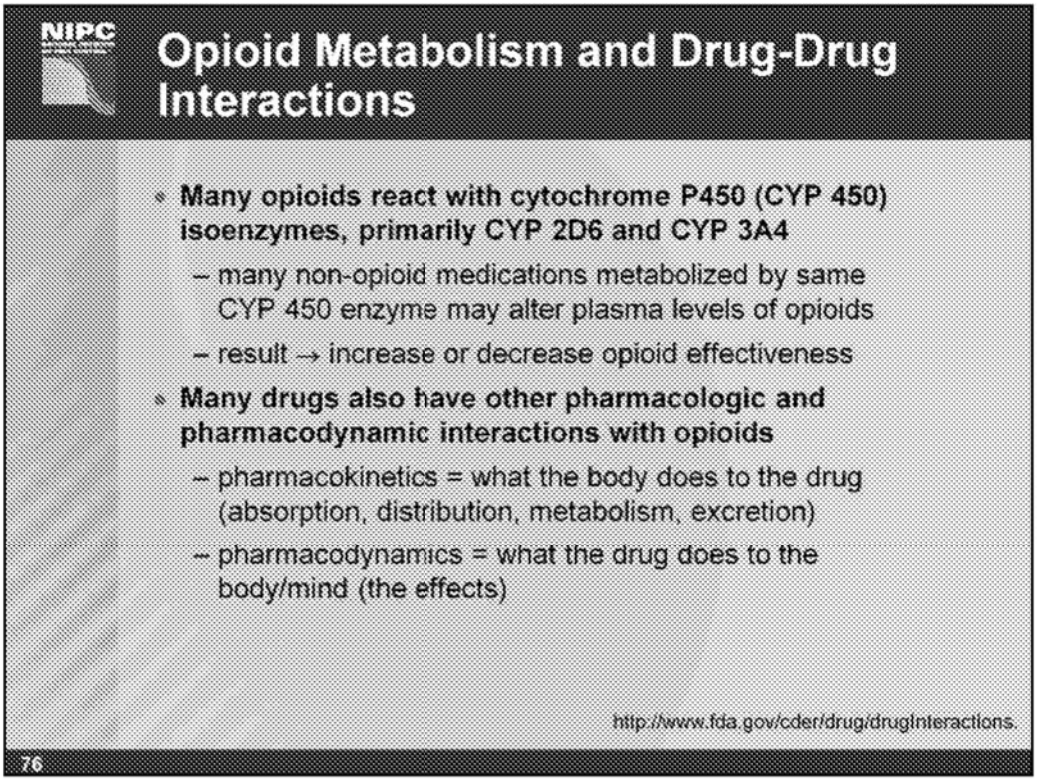
Evaluating for addiction in a patient who is prescribed long-term opioids for pain control is often problematic. While the concept of addiction may include the symptoms of physical dependence and tolerance, physical dependence and/or tolerance alone does not equate with addiction. In the chronic pain patient taking long-term opioids, physical dependence and tolerance should be expected, but the maladaptive behavior changes associated with addiction are not expected. The presence of these behaviors in the chronic pain patient is far more important in diagnosing addiction.

Savage SR. Assessment for addiction in pain-treatment settings. *Clin J Pain*. 2002;18(suppl 4):S28-S38.

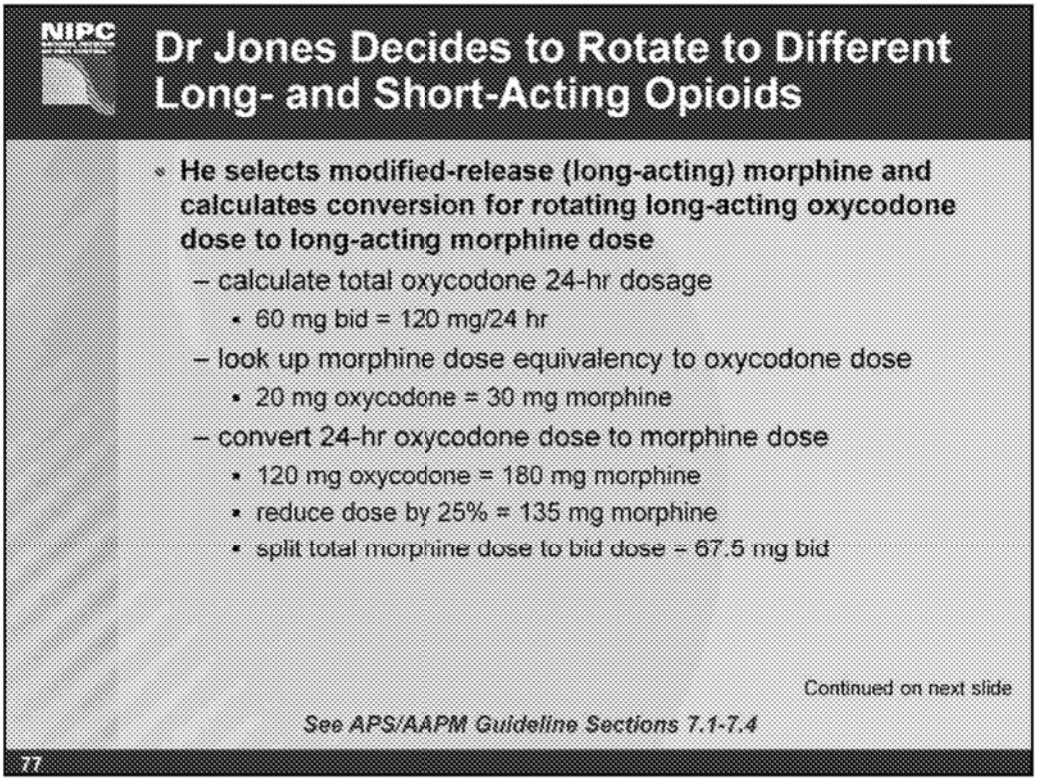
Sees KL, Clark HW. Opioid use in the treatment of chronic pain: assessment of addiction. *J Pain*

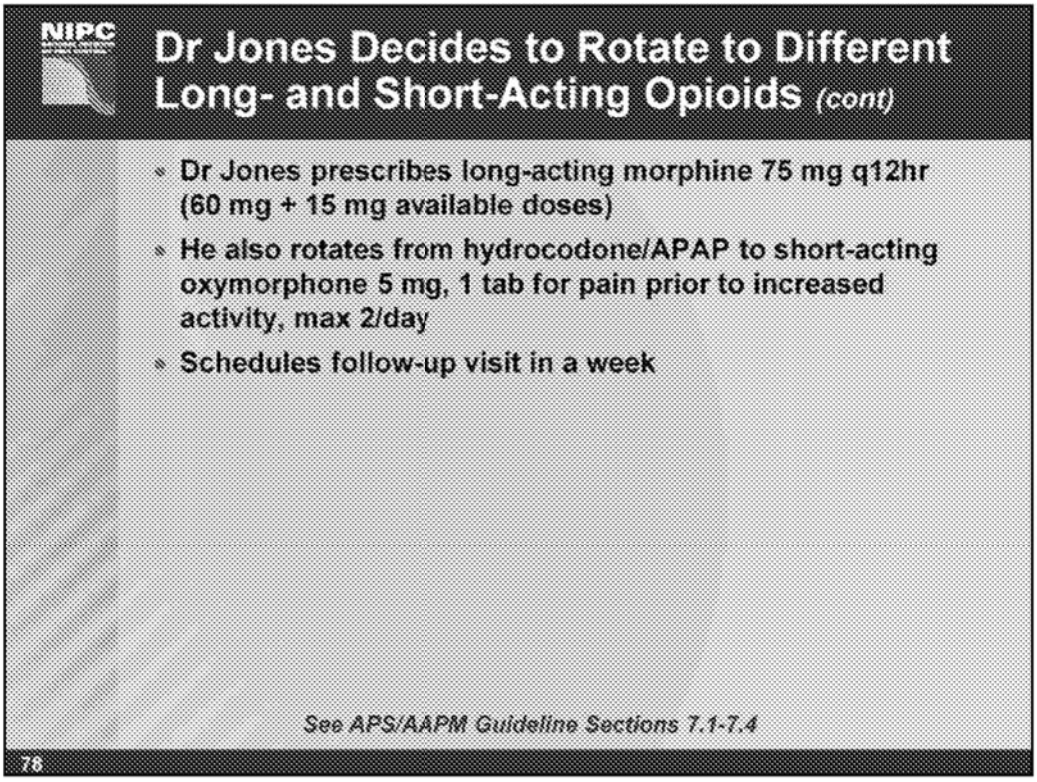
Symptom Manage. 1993;8:257-264.
American Academy of Pain Medicine, the American Pain Society and the American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain. *WMJ*. 2001;100(5):28-29.

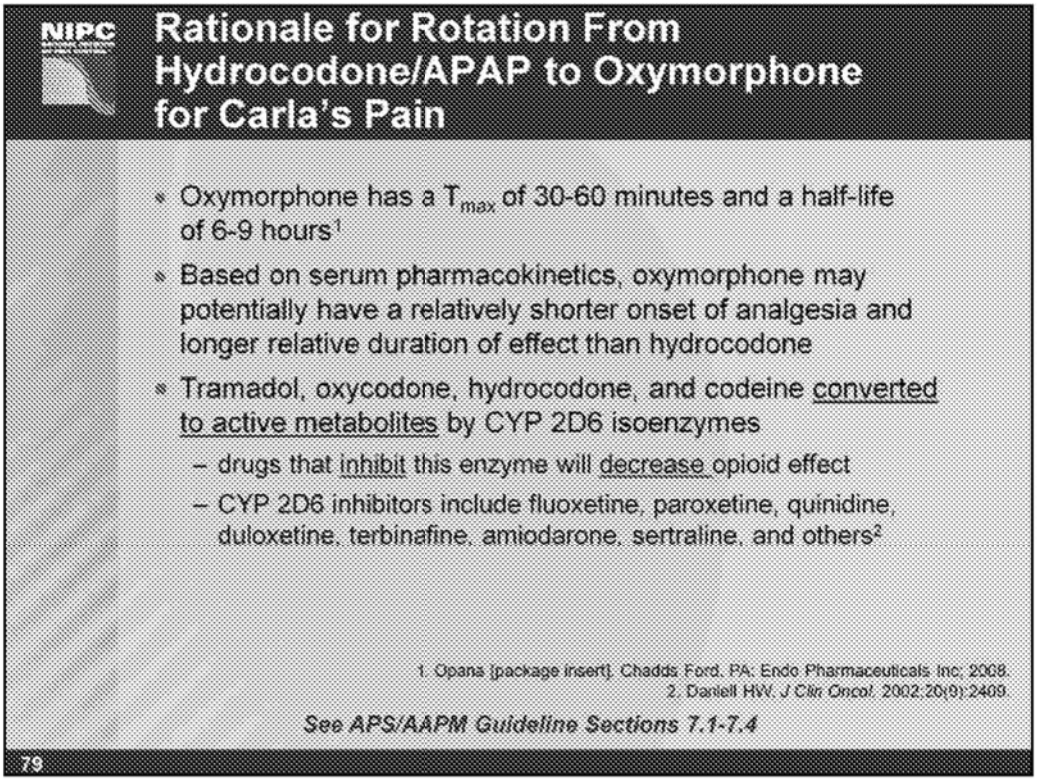

NIPC
What Dr Jones Told Carla
She may be developing tolerance
Continued physical therapy may help
She is not pacing herself appropriately at work
Pain may be due to multiple factors, including pharmacokinetics of concomitant medications
competition for CYP 2D6 enzyme by sertraline may reduce activity of hydrocodone (by reducing metabolism to active)
75



U.S. Food and Drug Administration. Drug Development and Drug Interactions. http://www.fda.gov/cder/drug/drugInteractions. Published May 1, 2006. Up-dated October 11, 2006.


NIPC
Dr Jones Decides to Rotate to Different Long- and Short-Acting Opioids
He selects modified-release (long-acting) morphine and calculates conversion for rotating long-acting oxycodone dose to long-acting morphine dose
– calculate total oxycodone 24-hr dosage
• 60 mg bid = 120 mg/24 hr
– look up morphine dose equivalency to oxycodone dose
• 20 mg oxycodone = 30 mg morphine
– convert 24-hr oxycodone dose to morphine dose
• 120 mg oxycodone = 180 mg morphine
• reduce dose by 25% = 135 mg morphine
• split total morphine dose to bid dose = 67.5 mg bid
Continued on next slide
See APS/AAPM Guideline Sections 7.1-7.4
77


NIPC
Dr Jones Decides to Rotate to Different Long- and Short-Acting Opioids (cont)
Dr Jones prescribes long-acting morphine 75 mg q12hr (60 mg + 15 mg available doses)
He also rotates from hydrocodone/APAP to short-acting oxymorphone 5 mg, 1 tab for pain prior to increased activity, max 2/day
Schedules follow-up visit in a week
See APS/AAPM Guideline Sections 7.1-7.4
78



To the Editor: The process of opioid selection for control of cancer pain, as recently outlined by Indelicato and Portenoy[1] in the January 1, 2002, issue of the *Journal of Clinical Oncology,* should include consideration of alterations in opioid effectiveness induced by concurrently administered medications. Codeine, hydrocodone, and oxycodone are only weak analgesics, and they may appropriately be characterized as prodrugs rather than drugs, until metabolized into the much more effective analgesic drugs morphine, hydromorphone, and oxymorphone under the influence of the cytochrome P-450 isoenzyme 2D6 (CYP 2D6).[2] The analgesic properties of morphine, hydromorphone, oxymorphone, propoxyphene, and fentanyl are largely due to their direct influence on opioid receptors and do not require additional metabolism, although the first metabolite of propoxyphene, norpropoxyphene, is also an effective analgesic with a very long half-life.

CYP 2D6 activity is genetically much diminished in 7% of whites, 3% of blacks, and 1% of Asians,[3] rendering oxycodone, hydrocodone, and codeine relatively ineffective analgesics in these "poor metabolizers."[4]

The activity of CYP 2D6 is also inhibited by most commonly prescribed selective serotonin reuptake inhibitors, including fluoxetine, fluvoxamine, paroxetine, sertraline, and bupropion,[5] medications that are commonly administered to cancer patients, as well as by quinine, quinidine, haloperidol, and amiodarone, which also are often administered to cancer patients for the treatment of concurrent conditions.

The CYP 2D6 inhibition resulting from these medications may last for several weeks after discontinuation of those with long half-lives. During this interval of decreasing inhibitor concentrations, inhibited metabolism of oxycodone and similar prodrugs may render them less effective analgesics than they would be after additional delay.

If the patient reported by Indelicato and Portenoy was consuming a CYP 2D6 inhibitor, her pain control while consuming oxycodone might have been more effective had the inhibitor previously been replaced for an appropriate period of time by another similar medication that did not inhibit this enzyme. If, on the other hand, the CYP 2D6 inhibitor was to be continued, initial analgesic rotation to a different opioid not requiring this enzyme system for its analgesic effectiveness would have been indicated.

Daniell HW. Inhibition of opioid analgesia by selective serotonin reuptake inhibitors. *J Clin Oncol.* 2002;20(9):2409.

1. Indelicato RA, Portenoy RK. Opioid rotation in the management of refractory cancer pain. *J Clin Oncol.* 2002;20:348-352.
2. Supernaw RB. CYP2D6 and the efficacy of codeine and codeine-like drugs. *Am J Pain Manage.* 2001;11:30-31.
3. Eichelbaum M, Gross AS. The genetic polymorphism of debrisoquine sparteine metabolism: Clinical aspects. *Pharmacol Ther.* 1990;46:377-394.
4. Lurcott G. The effects of the genetic absence and inhibition of CYP2D6 on the metabolism of codeine and its derivatives, hydrocodone and oxycodone. *Anesth Prog.* 1999;45:154-156.
5. Richelson E. Pharmacology of antidepressants. *Mayo Clin Proc.* 2001;76:511-527.

Opana [package insert]. Chadds Ford, Pa: Endo Pharmaceuticals Inc.; 2006

Vicodin package insert. http://www.rxabbott.com/pdf/vicodin.pdf. Up-dated March 2007.

NIPC

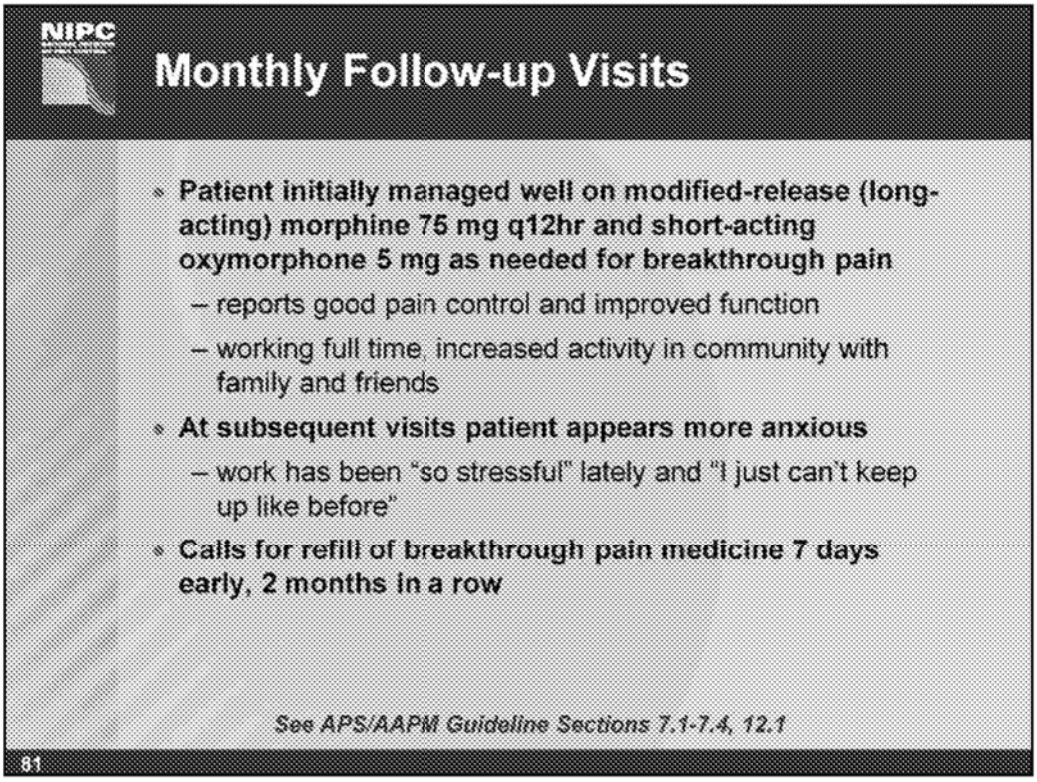
Carla: 1-Week Follow-up

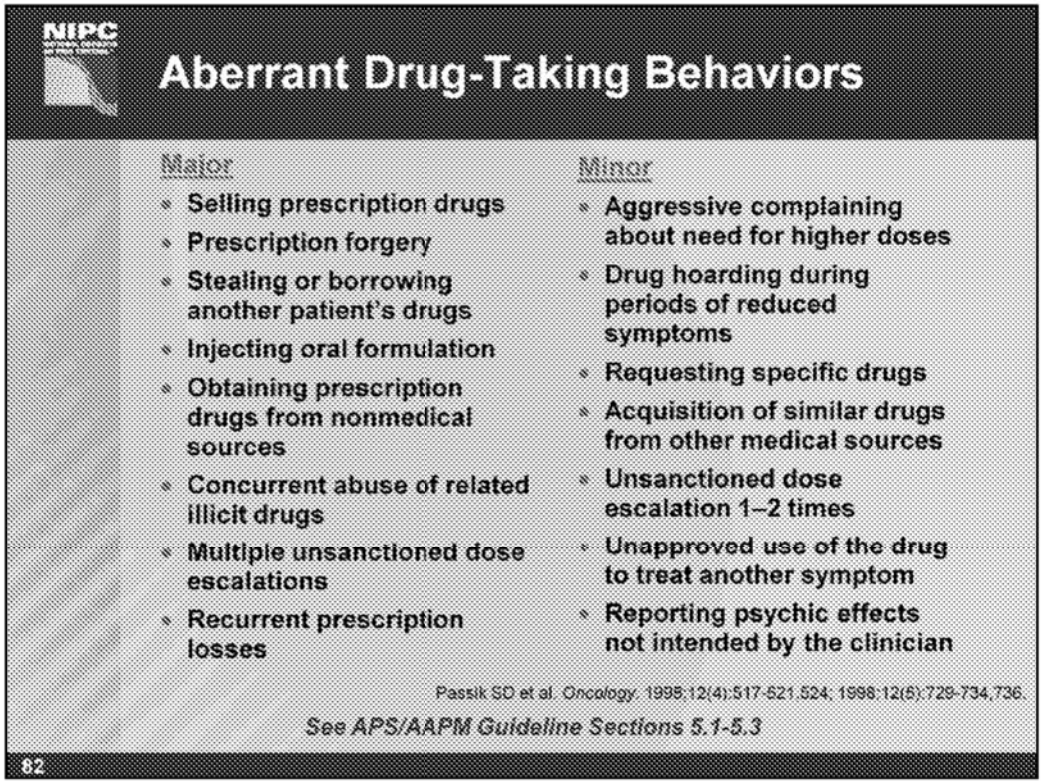
"A's" Reassessment Chart Note

- Analgesia: Reports good pain relief with new meds, average 3-4/10; breakthrough pain well controlled, no greater than 6/10 at end of workday
  - "It seems to work faster and last longer"
- AEs: None
- ADLs: Improved; able to walk entire mail route with tolerable level of pain
- Aberrant Drug-Taking Behavior: None, taking meds as Rx'd
- Assessment Impression: Good pain control on current dose, mood greatly improved, says sleeping well with better pain control
- Action Plan: Continue Rx as prescribed; follow-up monthly 3x, then reassess frequency of follow-up visits

See APS/AAPM Guideline Sections 5.1-5.3

80


NIPC
Monthly Follow-up Visits
Patient initially managed well on modified-release (long-acting) morphine 75 mg q12hr and short-acting oxymorphone 5 mg as needed for breakthrough pain
– reports good pain control and improved function
– working full time, increased activity in community with family and friends
At subsequent visits patient appears more anxious
– work has been "so stressful" lately and "I just can't keep up like before"
Calls for refill of breakthrough pain medicine 7 days early, 2 months in a row
See APS/AAPM Guideline Sections 7.1-7.4, 12.1
81



In assessing aberrant drug-taking behaviors in the context of the pain clinic setting, certain behaviors are probably more predictive of risk for true drug addiction problems than others.

Some of the more predictive behaviors, many of them illegal, include selling prescription drugs, forging prescriptions, stealing or borrowing another patient's drugs, injecting an oral formulation, obtaining prescription drugs from nonmedical sources, concurrent abuse of related illicit drugs, multiple unsanctioned dose escalations, or recurrent prescription losses.[1,2]

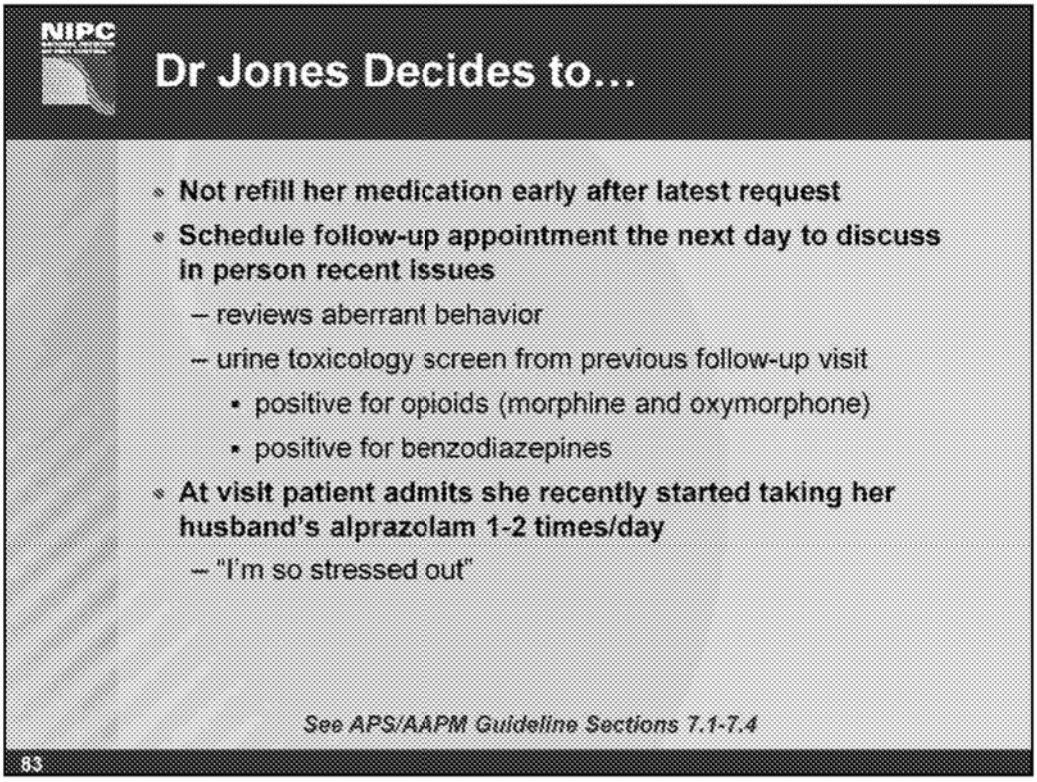
On the other hand, aberrant behaviors such as aggressive complaining about needing higher doses, drug hoarding, requesting specific drugs, acquisition of similar drugs from other medical sources, unsanctioned dose escalation on one or two occasions, unapproved use of the drug to treat another symptom, or reporting unintended psychic effects, may not be as predictive for drug abuse concerns.[1,2]

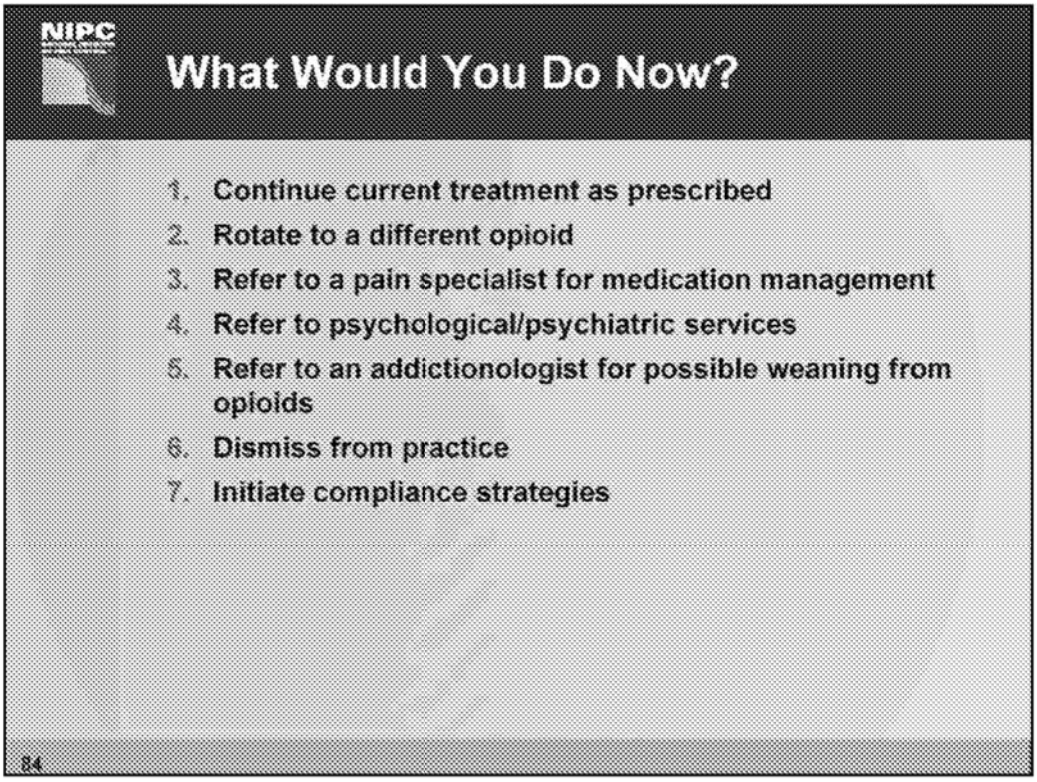
Because some degree of noncompliant behavior is common among patients in clinical practice, it is important to consider not only the type of behavior but also the frequency or number of aberrant behaviors occurring in an individual patient when assessing a potentially problematic situation.

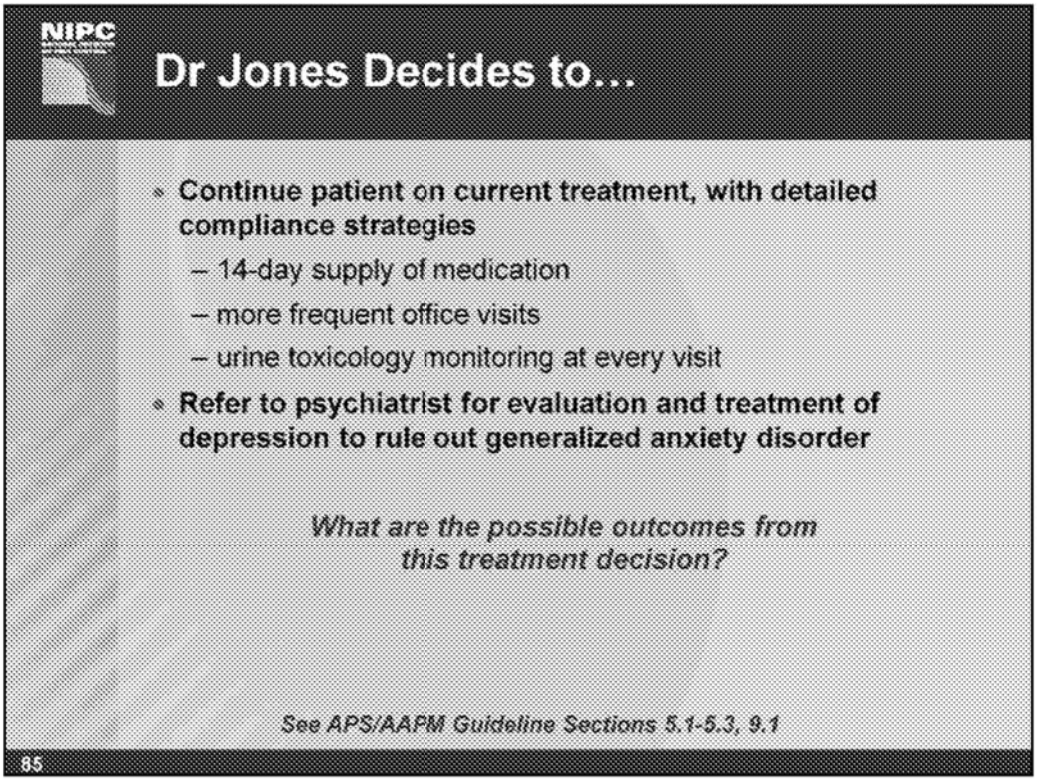
1. Passik SD, Portenoy RK, Ricketts PL. Substance abuse issues in cancer patients. Part 1: Prevalence and diagnosis. *Oncology*. (Huntingt). 1998;12(4):517-521, 524.

2. Passik SD, Portenoy RK, Ricketts PL. Substance abuse issues in cancer patients. Part 2:

Evaluation and Treatment. *Oncology*. (Huntingt). 1998;12(5):729-734, 736. 741-742.


NIPC
Dr Jones Decides to…
Not refill her medication early after latest request
Schedule follow-up appointment the next day to discuss in person recent issues
– reviews aberrant behavior
– urine toxicology screen from previous follow-up visit
• positive for opioids (morphine and oxymorphone)
• positive for benzodiazepines
At visit patient admits she recently started taking her husband's alprazolam 1-2 times/day
– "I'm so stressed out"
See APS/AAPM Guideline Sections 7.1-7.4
83


NIPC
What Would You Do Now?
1. Continue current treatment as prescribed
2. Rotate to a different opioid
3. Refer to a pain specialist for medication management
4. Refer to psychological/psychiatric services
5. Refer to an addictionologist for possible weaning from opioids
6. Dismiss from practice
7. Initiate compliance strategies
84


NIPC
Dr Jones Decides to…
Continue patient on current treatment, with detailed compliance strategies
– 14-day supply of medication
– more frequent office visits
– urine toxicology monitoring at every visit
Refer to psychiatrist for evaluation and treatment of depression to rule out generalized anxiety disorder
What are the possible outcomes from this treatment decision?
See APS/AAPM Guideline Sections 5.1-5.3, 9.1
85

NIPC

Possible Outcome: Good
Continued Follow-up

"A's" Reassessment Chart Note

- Analgesia: Good pain control, 3/10 baseline, 5-6/10 worst pain managed with breakthrough pain med
- AEs: None
- ADLs: Working full time; less anxious, active treatment w/psychiatrist & staff psychologist → better stress management
- Aberrant Drug-Taking Behavior: No early refill requests, taking breakthrough Rx as needed; no unprescribed meds in urine screen
- Assessment Impression: Learning relaxation techniques in therapy to apply at work and home; started home exercise program; says she's "doing great"
- Action Plan: Continue current treatment regimen

See APS/AAPM Guideline Sections 5.1-5.3, 7.1-7.4

86

NIPC

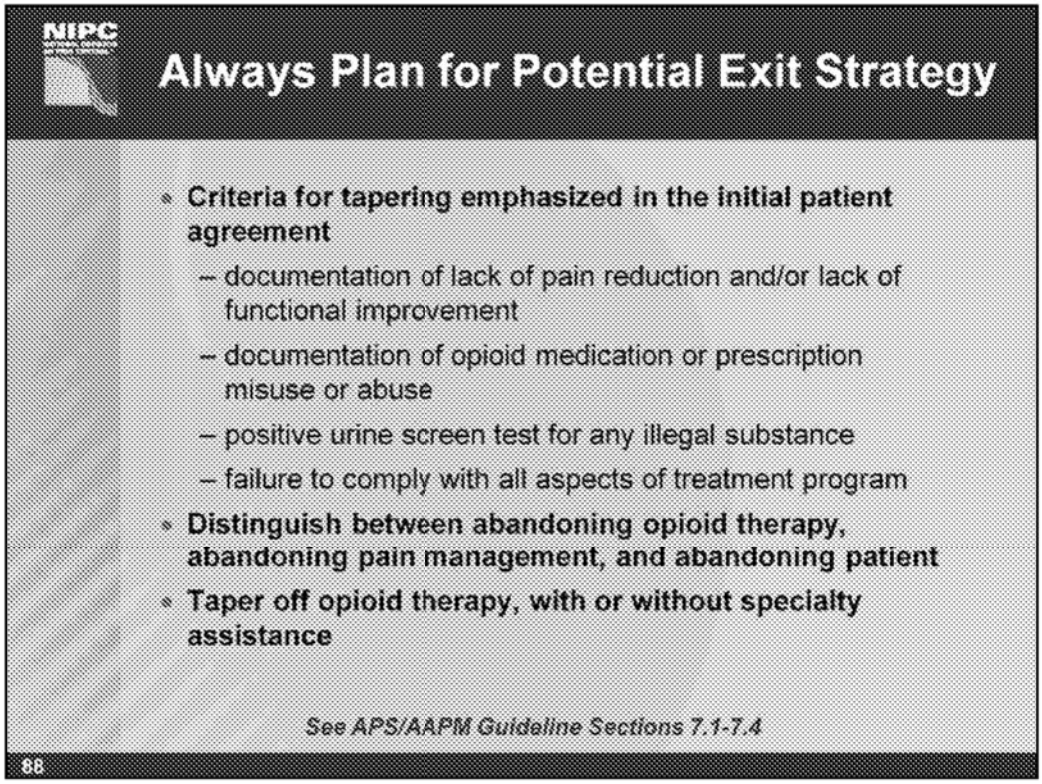
Possible Outcome: Bad
Patient Calls for Early Refill, Again

"A's" Reassessment Chart Note

- Analgesia: Patient complains of poor pain control especially when walking. "I need more pain meds—my pain is 12/10"
- AEs: None
- ADLs: Only able to work half a day several times a week, missing work more frequently, increased down time at home
- Aberrant Drug-Taking Behavior: Several early refill requests; not compliant with physical therapy or psychology visits; phone message from Urgent Care Center of patient requesting pain medicine
- Assessment Impression: Chronic S1 radiculopathy, opioid management noncompliance, possible opioid addiction vs opioid-nonresponsive pain syndrome
- Action Plan: Not a candidate for opioid therapy, taper from opioids in consultation with addictionologist; consider interventional therapy and refer to psychology/psychiatry services for more intensive evaluation/treatment

See APS/AAPM Guideline Sections 5.1-5.3, 7.1-7.4, 9.1, 11.1-11.2

87



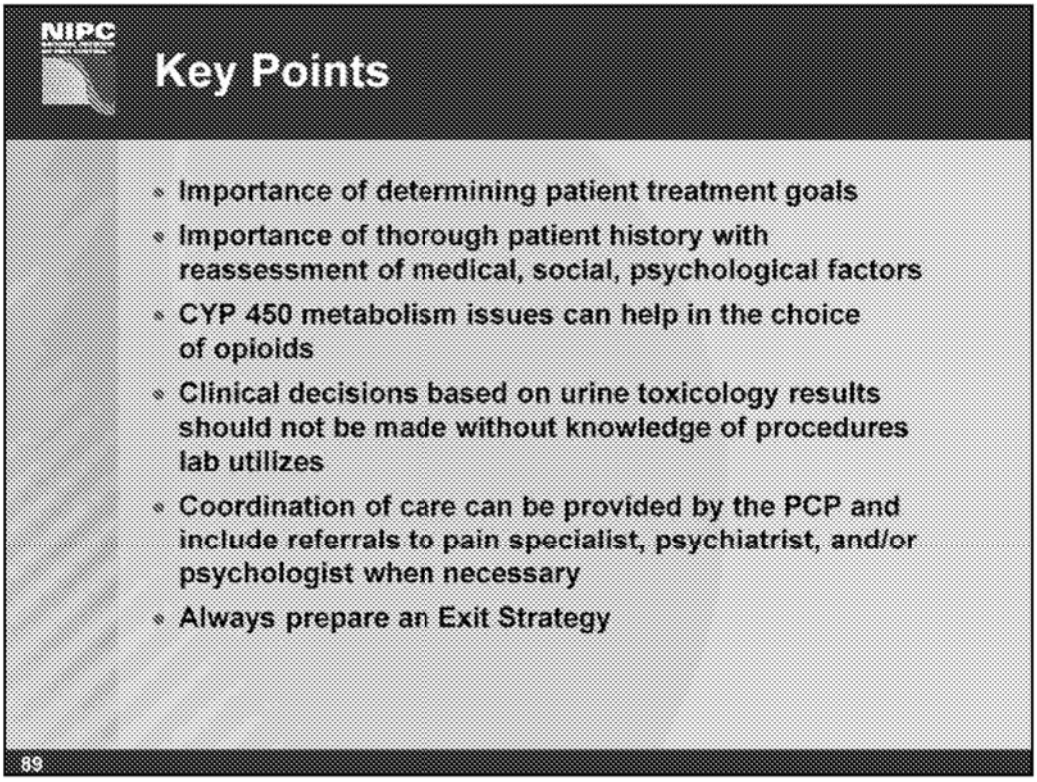
It is essential that an exit strategy be discussed with the patient when initiating a trial of opioid therapy.

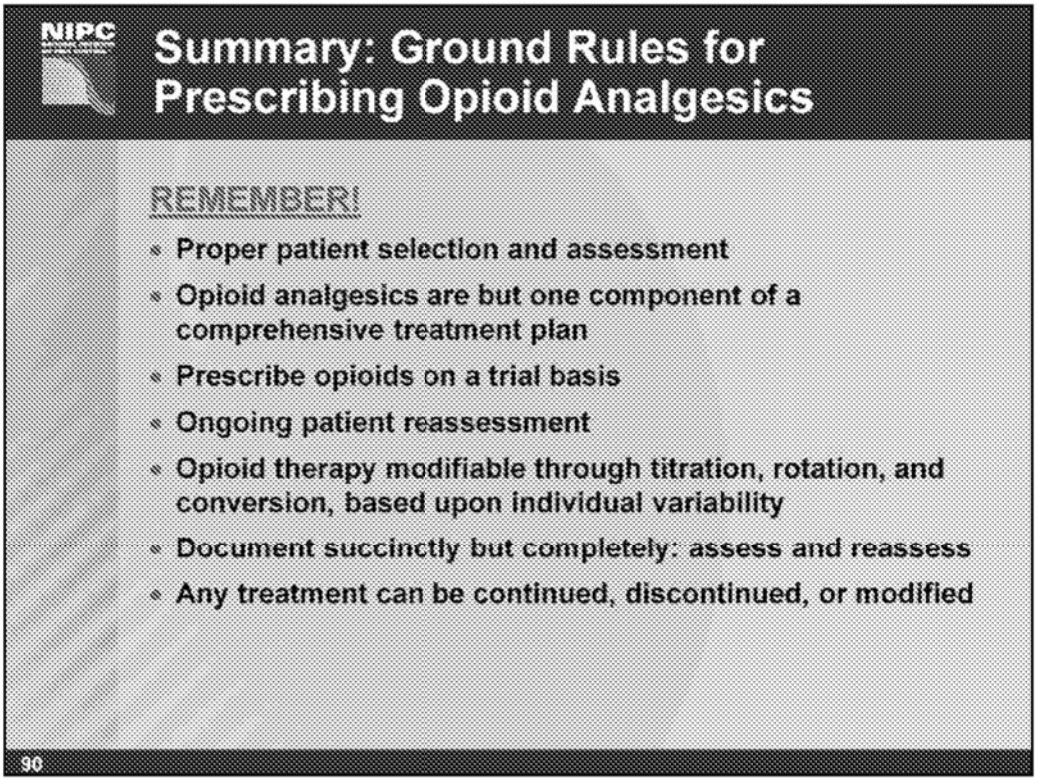
When physicians begin treatment, they should also begin to think about an exit strategy. They should ask these questions: When do you back off? When do you say that the treatment has failed and that this patient should not be given opioids anymore?

Physicians should talk about the difficult decisions before starting the treatment. In this way, they avoid issues of abandonment later on.

For example, patients can be told: "If your function doesn't improve on medication, we're going to talk about taking you off the medication in a week or in a month. If things don't get better, I'm going to withdraw you from this acetaminophen/hydrocodone combination." If the patient understands this, in a month when the physician says, "The hydrocodone/acetaminophen compound didn't work, so let's taper you off," there will not be issues of abandonment, because you have already discussed this strategy with the patient.

A simple **exit strategy algorithm** has been developed and is available for downloading from the Opioid Analgesia Tool Kit at PainKnowledge.org. The algorithm will guide you in identifying the opioid non-responder, and in broad terms, what your options are for tapering the patient off opioid therapy.


NIPC
Key Points
Importance of determining patient treatment goals
Importance of thorough patient history with reassessment of medical, social, psychological factors
CYP 450 metabolism issues can help in the choice of opioids
Clinical decisions based on urine toxicology results should not be made without knowledge of procedures lab utilizes
Coordination of care can be provided by the PCP and include referrals to pain specialist, psychiatrist, and/or psychologist when necessary
Always prepare an Exit Strategy
89


NIPC
Summary: Ground Rules for Prescribing Opioid Analgesics
REMEMBER!
Proper patient selection and assessment
Opioid analgesics are but one component of a comprehensive treatment plan
Prescribe opioids on a trial basis
Ongoing patient reassessment
Opioid therapy modifiable through titration, rotation, and conversion, based upon individual variability
Document succinctly but completely: assess and reassess
Any treatment can be continued, discontinued, or modified
90